# CLINICAL PROFILE AND ANTIBIOTIC USE IN CHILDREN WITH ENTERIC FEVER

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*Dedicated*

*To*

*adorable sister*

*Isha Joshi*

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Dr. Disha Joshi

# LIST OF ABBREVIATIONS

| | |
|---|---|
| I/V | Intravenous |
| MDR | Multi Drug Resistant |
| XDR | Extensive Drug Resistant |
| SD | Standard Of Deviation |
| TLC | Total Leucocyte Count |
| MCV | Mean Corpuscular Volume |
| SGOT | Serum Glutamic-Oxaloacetic Transaminase |
| SGPT | Serum Glutamic Pyruvic Transaminase |
| LDH | Lactate Dehydrogenase |
| CRP | C Reactive Protein |
| ESR | Erythrocyte Sedimentation Rate |
| $2^{ND}$ | Second |
| $3^{RD}$ | Third |
| S | Sensitive |
| R | Resistant |
| % | Percentage |
| DOR | Discharge On Request |
| N | Number |
| NO | Number |
| OPD | Out Patient Department |
| MIC | Minimum Inhibitory Concentration |
| S.TYPHI | Salmonella Typhi |
| S.PARATYPHI | Salmonella Paratyphi |
| CLSI | Clinical And Laboratory Standards Institute |
| PCR | Polymerase Chain Reaction |
| CFTR | Cystic Fibrosis Transmembrane Conductance Regulator |

| | |
|---|---|
| EEG | Electroencephalogram |
| WHO | World Health Organization |
| TCV | Typhoid Conjugate Vaccine |
| MG | Micro Gram |
| ML | Milli Litre |
| L | Litre |
| MG | Milligram |
| LTD. | Limited |
| NARST | Nalidixic Acid Resistant Salmonella Typhi |

# ABSTRACT

**INTRODUCTION:** Enteric fever is a community acquired systemic infection which is more common in resource-limited overcrowded communities with poor access to sanitation and its management is compounded by the increasing antimicrobial resistance to the first-line antibiotics used .

**AIM OF STUDY:** 1)To study clinical profile of children with Enteric Fever.
2) To study Antibiotic use and outcome in children with Enteric Fever.

**MATERIALS & METHODS:** This descriptive study was conducted in the departments of Pediatrics and Microbiology, Dayanand Medical College and Hospital, Ludhiana, Punjab, Indiafrom month of February 2020 to month of August 2021.All inpatients who meet the confirmed case definition with Blood Culture positive for Salmonella and Probable case definition with clinical findings and serodiagnosis based on Widal test were included . Those inpatients who did not meet case definition and did not give consent were excluded. Clinical profile of all cases and antibiotic sensitivity pattern in culture positive cases and use of antibiotics as per sensitivity profile and its impact on duration of hospital stay , deffervesence of fever and outcome was studied .

**RESULTS:** 70 cases were enrolled, 40% females and 60% males, maximum cases 52.9% in age group of more than 60 months. All had fever at admission , moderate grade in 52.9% , 31.4% had pain abdomen and 50% had loose stools and vomitings as associated symptoms .Serodiagnosis was done by Widal test which had 80% sensitivity and had positive predictive value . Salmonella Typhi Isolates were seen in 74.3% cases and Paratyphi Isolates in 12.9% cases. Both Salmonella Typhi and Paratyphi isolates were 100% sensitive to azithromycin and ceftriaxone . Salmonella Typhi was more resistant to Quinolones and cefixime whereas Paratyphi isolates were more resistant to Ampicillin and Cefuroxime in comparison .No MDR case was found. 88.1% cases were given i/v ceftriaxone and 20% cases had day of deffervesenceby day 14 of onset of fever .Combination antibiotics did not affect the outcome and all cases were discharged .

**Conclusion**: Clinical profile and antibiotic sensitivity pattern studies of Enteric fever cases had impact on selection ofantibiotics. Ceftriaxone , Cotrimoxazole and Azithromycin being 100% sensitive and increasing resistance to quinolones , ampicillin and cefuroxime.Further study is required to find MDR and XDR Salmonella isolates .



**KEYWORDS:** Enteric fever, children, salmonella, blood culture, widal test , MDR , Ceftriaxone , Azithromycin .

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# INTRODUCTION

Enteric fever is a community-acquired systemic infection which continues to be a public health problem in developing countries. It is more common in resource-limited overcrowded communities with poor access to sanitation.[1]

The problem in the management of enteric fever is compounded by theincreasing antimicrobial resistance to the first-line antibiotics used for theenteric fever [2] Enteric fever is common infection with challenges of antimicrobialresistance.[3]

Salmonella enterica serotype typhi is a gram-negative bacterium that is responsible for typhoid fever and has been a burden on developing nations for generations. In 1829, Pierre Louis was the first to coin the term “typhoid fever” after identifying lesions in the abdominal lymph nodes of patients who had died from “gastric fever.”[4] The term was derived from the Greek word “typhus” which meant **“**smoky” and was used to describe the delirium that patients would exhibit with the disease.[4] Although first described in the early 1800s, it was not until 1880 when the organism for typhoid fever was discovered.[4] In 1880, German pathologist Karl Eberth identified S. enterica. It was first cultured in 1884 by Georg Gaffky.

Salmonella enterica serotype typhi is a gram-negative, rod-shaped, flagellated bacterium whose only reservoir is the human body[5] The bacterium is serologically positive for lipopolysaccharide antigens O9 and O12 as well as the distinct polysaccharide capsular antigen Vi[5] Antigen Vi-negative strains appear to be less infectious and less virulent as compared to those strains that are Vi positive.[5]

**Pathophysiology**

Salmonella enterica serotype typhi is usually contracted by ingestion of food or water that is contaminated with the excrements of people that carry the organism and must survive the gastric pH barrier in the stomach prior to adherence in the small intestine.[6] An infectious dose

of Salmonella enterica serotype typhi in healthy individuals ranges between 1000 and 1 million organisms but can be related to the host's defense mechanisms.[6]

Salmonella enterica serotype typhi enter the submucosal region of the small bowel by either direct penetration into the epithelial tissue mediated by the cystic fibrosis transmembrane conductance regulator (CFTR) or via the M-cell, a specialized lymphoid epithelial cell. Once within the submucosa, the bacterium causes hypertrophy of the Peyer's patches.[6]

Dissemination of the organism from the Peyer's patches occurs via the lymphatic system and the bloodstream.6 Cellular replication within the reticuloendothelial system is a hallmark of the disease and eventually causes the systemic symptoms that a clinician will observe.[6] Following replication, organisms will reside in the macrophages of the liver, spleen, and bone marrow.[6] Classically, Salmonella enterica serotype typhi can be cultured from the bone marrow even after anti-microbial therapy has been initiated.[6]

Approximately 1% to 5% of patients will become chronic carriers of Salmonella enterica serotype typhi despite adequate antimicrobial therapy.[6] A chronic carrier is defined as a patient that has excretion of the bacterium in the stool or urine for greater than 12 months after an acute infection and is typically of the female gender or has cholelithiasis.[6] Those in the chronic carrier state will typically have high levels of antibodies to the Vi antigen and will not develop the clinical disease. The most famous of these chronic carriers was Mary Mallon who was diagnosed as a "healthy carrier" of the disease in 1906 after transmitting the disease to several households in which she served as the cook. The term "Typhoid Mary" became prominent during public health campaigns and is still used in modern culture today.

**The clinical features** of pediatric enteric fever are nonspecific and overlap with a variety of infective etiologies in endemic settings.[7] The

proportion of cases clinical suspected with enteric fever may be as low as 4% at initial presentation in ultimately blood culture–confirmed cases in children Clinical features, complications, and outcomes differ between adults and children. A recent systematic review of clinical and laboratory features of enteric fever indicated that the risk of mortality from enteric fever is 4 times higher in children <5 years compared with those >5 years of age.[7]

**Generalized Systemic Features**

A typical febrile response usually occurs between 5 and 15 days after exposure to the organism as demonstrated in the challenge model in adult subjects.[7]Evidence from a recently published systematic review reported that fever is a consistent feature of pediatric enteric fever, in 97%–100% of cases [7], not uncommonly being the sole manifestation, presenting as a fever of unknown origin with inconclusive laboratory results. The widespread and poorly regulated use of antibiotics and antipyretics in low- to middle-income country settings not only confounds the clinical picture but also serves for the origin and propagation of MDR strains of Salmonella. If untreated, the febrile response reaches its peak in the second week of illness in a characteristic “stepladder” pattern .Chills and rigors are 4 times more common in adults than in children.[7] Relative bradycardia, a classical finding in enteric fever, is identifiable in 11%–30% of children and appears to be 15 times more likely to occur in African children than the children in Asia.[7]

**Gastrointestinal Features**

Gastrointestinal (GI) manifestations of acute enteric fever are variable in children. Diarrhea is seen >2.5 times more commonly in enteric fever affected infants than in older children and adults. A lesser proportion of children may have constipation, which has been associated with disease relapse in children infected with MDR strains, according to observations from a single-center study over a 15-year period. GI bleeding and perforation, though rare, have been known to occur in children and are 9 times higher in hospital-based studies than

community-based settings [7], possibly reflecting a sampling bias of severe cases being referred to hospital from the community. Predictors of death due to perforation in children include older age, high temperature, postoperative anastomotic leak, and fecal fistula. A robust immune response coupled with well-primed Peyers patches are main requirements for these complications, which increase with the increasing age of the child, and this is possibly why severe complications are seldom seen in the younger age groups. Paralytic ileus is more commonly observed in infants and young childrenbeing 7 times more likely in African children than their Asian counterparts, according to Azmatullah et al [7 )Abdominal pain and nausea, which are commonly seen in adults, are also seen in older children but are difficult to determine in young children.

**Neurological Features**

The occurrence of seizures in enteric fever is more common in children than adults. The high temperatures associated with enteric fever induce febrile seizures in susceptible children between 6 months and 5 years of age. The occurrence of febrile seizures may account for the higher seizure rate described in children. It is not clear whether Salmonellahas a direct effect on the central nervous system, as the bacteria are seldom isolated from cerebrospinal fluid during lumbar puncture. Nevertheless, the toxin released by the bacteria may elicit cortical irritation. The typhoid toxin only binds to mammalian cell membranes, made up of glycoproteins containing Neu5Ac-terminated glycans, which are also found in gangliosides that are components of the neuronal cell membrane in the brain. The toxin could therefore cause membrane depolarization by presumably interfering with the voltage-gated sodium channels. Further work needs to be done to establish the mechanism at the cell membrane level; however, a distinct frontal intermittent rhythmic delta activity pattern on electroencephalogram (EEG) has been reported in Salmonella encephalopathy. This EEG pattern has been associated with the manifestation of seizures. Secondary causes such as

hyponatremia and hypoglycemia due to salt and water loss from the gut may be contributing factors. Other neurologic complications, rarely encountered [7] but predominantly described in the pediatric age group, include acute cerebellar ataxia, sinus thrombosis, meningism, cerebritis, pseudo tumor cerebri, encephalopathy, brain abscesses, and Guillain-Barré syndrome. Neuropsychiatric changes, delirium, insomnia, and coma are also described in children but are more frequent in adults.

**Hepatosplenic Features**

A clinically tender hepatomegaly and splenomegaly are seen in up to 85 percent and 90 percent cases respectively, of pediatric enteric fever cases. Typhoid hepatitis or “hepatitis typhosa” is more frequently seen in younger children but assumes importance as it mimics acute viral hepatitis in the tropics and is likely to either be immunologically mediated or due to the direct effects of the typhoid toxin on the hepatocytes. Acalculous cholecystitis has also been described in brief reports and occurs predominantly in younger children.[7] Hepatic and splenic abscesses with a subsequent splenic abscess rupture are more commonly encountered in younger children, the immunosuppressed, and those with hemoglobinopathies. Splenic rupture, a devastating complication, though uncommon in children, is particularly associated with MDR infection, although it is not clear whether this occurs due to treatment failure or virulence of the pathogen.

**Cardiopulmonary Features**

Case reports and expert reviews describe cardiac complications such as myocarditis, endocarditis, pericarditis, and pericardial effusion, which are more common in older children and adults with risk factors such as congenital heart disease, rheumatic heart disease, and valvular defects. Respiratory symptoms may dominate the clinical picture of pediatric enteric fever, with cough being the most common manifestation seen in up to 72% of cases A clinical picture of bronchopneumonia, one of the respiratory complications of enteric fever, also occurs occasionally and is twice as common in children than

in adults.[7] A clinical picture of reactive airway disease with auscultatory rhonchi and occasional crepitations may be noted in younger children. Risk factors for complications such as pleural effusion, empyema, and bronchopleural fistulas though seldom reported in children, may occur in those with previous respiratory infections, sickle cell anemia, and immunosuppression.

**Renal Features**

Renal involvement with enteric fever is noticed onlyin 2-3% of the cases. The common complications of typhoid related to the urinary tract include cystitis,pyelitis, pyelonephritis and mild proteinuria. Differentmechanisms can lead to renal involvement in typhoid fever. Dehydration not managed correctly may lead to acute tubular necrosis. Other renal manifestations like Immunoglobulin A (IgA) nephropathy, hemolytic uremic syndrome and Henoch- Schonlein purpura may also occur. Acute interstitial nephritis and acute tubular dysfunction secondary to Salmonella typhimurium has been reported in children and adults either in isolation or with schistosomiasis. Renal failure secondary to rhabdomyolysis has also been reported.

Glomerulonephritis is uncommon. Immune complex glomerulitis, with deposition of immunoglobulins and C3 globulin, is seen in these patients. Salmonella Vi antigen was also found in the glomerular capillary wall, suggesting the direct role of Salmonella typhi in the pathogenesis of the glomerular lesion. The present case showed diffuse proliferative glomerulonephritis in renal biopsy. Buka et al., showed patients with typhoid nephritis compared to post- streptococcal glomerulonephritis (PSGN) have edema for prolonged periods before admission, are likely to be febrile and have splenomegaly. C3 levels are lower in PSGN patients Renal involvement with enteric fever is noticed only in 2-3% of the cases. The common complications of typhoid related to the urinary tract include cystitis, pyelitis, pyelonephritis and mild proteinuria. Different mechanisms can lead to renal involvement in typhoid fever. Dehydration not managed correctly

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**Hematological Features**

The transient pancytopenia seen in acute illness may, in part, be explained by seeding of Salmonella to the bone marrow. A systematic review suggests that during an episode of enteric fever, children in Africa have a 5 times greater risk of severe anemia and a 15 times greater risk of thrombocytopenia than children in Asia . Further evidence is required to confirm whether S. Typhi causes these

hematological abnormalities independently and to what extent the host genetics play a role. As a facultative intracellular gram-negative organism, Salmonella induces apoptosis in the macrophages that it infects, contributing to the leukopenia. Eosinopenia in particular is an important indicator of disease severityat may be seen in up to 70% of children with enteric fever and has been well documented in adult patients as well as in the human challenge model Supplementary Reference 39]. On the other hand, and contrary to the leukopenia seen in adults, a peculiar finding in children is the relatively common occurrence of leukocytosis or the presence of a leukocyte count within the normal range.[10]In fact, leukocytosis is almost 3 times more likely to occur in children than in adults, while children under 5 are >4 times more likely to have an elevated leukocyte count than older children. Butler et al observed a strong association of a leukemoid response with shigellosis which was possibly induced by the lipopolysaccharide present in gram-negative bacilli, which might also be the case in enteric fever. Rare hematologic complications reported in enteric fever include disseminated intravascular coagulation, hemophagocytosis, bone marrow suppression, and bone marrow granulomata, all of which are more commonly described in adults than in children.[7]

**Prevalance**

Salmonella Typhi is the leading cause of enteric fever cases responsible for between 12 and 21 million illness episodes and over 140,000 deaths each year globally.[11,12] The disease is largely prevalent in the low and middle income countries of South Asia. Three community-based cohort studies conducted between 1995 and 2006 in India estimated the incidence of culture confirmed typhoid at 377 (178–801) per 100,000 person years with the highest incidence in early childhood.[13,14] The **burden of enteric fever** is predicted to worsen with the emergence of multi-drug resistant strain H58 in this region.

The World Health Organization (WHO) in its position paper on typhoid published in 2008 recommends the use of typhoid vaccines to prevent infection in high-risk populations, particularly where antibiotic

resistance is prevalent. These recommendations have remained unimplemented in India partly due to a perceived decline in the incidence and severity of typhoid fever in recent hospital-based reports accompanied with evidence of heterogeneous distribution of disease. These findings of declining disease burden in hospital based studies can partly be attributed to the indiscriminate early use of antibiotics to treat febrile illness. Newer antibiotics, that are increasingly accessible over the counter, have been shown to decrease transmission of this host-restricted organism when administered appropriately, early in disease.[15,16] Furthermore, antibiotics decrease culture confirmation by achieving defervescence in ambulatory care where cultures are generally not performed and by decreasing the sensitivity of blood culture post antibiotic therapy. In the absence of an alternative diagnostic assay of sufficient diagnostic accuracy, estimation of disease burden continues to rely on isolation of the organism by blood culture that is likely to be influenced by prior treatment and healthcare seeking behaviour.

While it is challenging to disaggregate the complex interplay between antimicrobial use, antimicrobial susceptibility and disease burden, estimating age-specific incidence of typhoid in the community by investigating febrile episodes prior to antimicrobial therapy will provide a better understanding of current disease burden and its transmission dynamics.

Typhoid is spread by infected human waste, so safe food, clean water, improved sanitation, and good hygiene (WASH) practices are key to preventing the disease. Because of the significant burden of typhoid and the growing threat of drug resistance, the role of vaccines alongside WASH interventions is critical in high-risk, typhoid-endemic areas. This is especially important among rural and hard-to-reach communities where progress in medical services, infrastructure, and development may be slow. Additionally, typhoid vaccines are valuable

for travelers, food workers (including street vendors), household contacts of typhoid carriers, and laboratory workers.

**Currently available typhoid vaccines**

Three classes of typhoid vaccines are currently recommended by the World Health Organization (WHO).

Typhoid conjugate Vaccine which comes under trade name Typbar TCV (Bharat Biotech) TYPHIBEV (Biological E) is given at age > 6 months of age, 1 dose, i.m with effectiveness > 80 % and duration of protection >3 years . Whereas Vi Capsular polysaccharide vaccine which comes under tradename Typhim Vi® (Sanofi Pasteur) Typherix (GlaxoSmithKline) is given at > 2years of age,i/m, 1 dose with boosters every 2 to 3 years with duration of protection 2 years and effectiveness 50 % to 80 % .Oral capsules under tradename Vivotif® (PaxVax) are also available for > 6 years of age with effectiveness 50 %– 80 %. 3 to 4 doses are given with 7 years of duration of protection.

Uptake of the Ty21a and ViCPS vaccines in typhoid-endemic countries has been low. The Ty21a vaccine requires numerous doses, and the ViCPS vaccine has short-lived protection. Additionally, neither vaccine is amenable to use in children younger than two years of age, which limits the potential health benefits and prevents use in routine childhood vaccination programs. Gavi, the Vaccine Alliance does not provide funding for Ty21a or ViCPS vaccines.

New typhoid conjugate vaccines (TCVs) address the limitations of prior vaccines. These vaccines are of particular interest to the global health community because TCVs have the potential to overcome many of the challenges that impeded uptake of earlier vaccines, including longer-lasting protection*, fewer doses, and suitability for children younger than two years of age, allowing for inclusion in routine childhood immunization programs. Many TCVs are under development, and four have been licensed in India.

Typbar TCV, manufactured by Bharat Biotech Ltd., was prequalified by WHO in late 2017 and recommended by WHO in 2018. It is administered in a single dose and approved for children six months of age and older.

TYPHIBEV, manufactured by Biological E, was prequalified by WHO in late 2020. It is administered in a single dose and approved for children over six months of age. Clinical studies show that it is safe when given at 9 months of age concurrently with measles vaccine, and its immune response profile is similar to that of Typbar TCV.

Another advanced TCV candidate is called PedaTyph™, which is manufactured by Bio-Med and is licensed in India for children three months of age and older. Efficacy trials of PedaTyph have found more than 90 percent efficacy against typhoid. However, it has not been submitted for WHO prequalification. Seven other TCV candidates are in various stages of development.

**World Health Organization recommendations**

The WHO position paper on typhoid vaccines, published in 2018, states:

WHO recommends programmatic use of typhoid vaccines for the control of typhoid fever. Among the available typhoid vaccines, TCV is preferred at all ages in view of its improved immunological properties, suitability for use in younger children and expected longer duration of protection. Countries may also consider the routine use of ViPS vaccine in individuals aged 2 years and older, and Ty21a vaccine for individuals aged more than 6 years. In choosing a typhoid vaccine, the costs, programmatic issues and duration of protection should be considered.

WHO recommends the introduction of TCV to be prioritized in countries with the highest burden of typhoiddisease or a high burden of antimicrobial resistant S. Typhi. Decisions on the age of TCV

administration,target population and delivery strategy for routine and catch-up vaccination should be based on the localepidemiology of typhoid fever, including antimicrobial resistance patterns, and programmatic considerationsof the routine childhood immunization programme.

The problem in the **management of enteric fever** is compounded by the increasing **antimicrobial resistance to** the first-line antibiotics used for the enteric fever. Multidrug-resistant strains were prevalent worldwide and had previously caused outbreaks in India

NARST Nalidixic Acid Resistant Salmonella typhi, with decreased susceptibility to ciprofloxacin (0.125-1 µg/L) causing therapeutic failure, has emerged worldwide and became endemic in the Indian subcontinent. Consequently, high-level ciprofloxacin-resistant enteric fever evolved in the Asian countries, including India.[18]Contrary to this, a high-level fluoroquinolone resistance in non-enteric fever salmonellae has reported frequently; with minimum inhibitory concentration (MIC) ranging from 16 to 64 µg/mL.[19]

The quinolones used in therapy of enteric fever are ciprofloxacin, gatifloxacin, levofloxacin and ofloxacin. Study done on 31 ciprofloxacin-resistant isolates of enteric fever, on E-strip MIC testing, all the isolates showed an MIC ≥ 32 µg/mL.[20]

Expanded-spectrum cephalosporins, such as cefipime, cefpodoxime proxetil, ceftriaxone and cefixime, have shown promise as therapies for the treatment of enteric fever. However, only cefixime and cefpodoxime proxetil have oral route of administration, while ceftriaxone and cefipime have parenteral route. Also, cefpodoxime proxetil has a favorable pharmacokinetic profile, which allows twice-daily administration. Cefixime and cefpodoxime are oral, but the cost of cefpodoxime is less than that of cefixime. Resistance is also emerging to extended-spectrum cephalosporins: ceftriaxone, cefixime, cefipime.[21] These alternative regimens have several disadvantages: their high costs, intravenous route of administration and prolonged

defervescence time. In another study amongst the cephalosporins tested, cefotaxime, a parenteral third-generation cephalosporin, demonstrated better results as it had the least MIC50 and MIC90, compared to oral third-generation cefixime and parenteral fourth-generation cefipime

**Newer Drugs For Enteric Fever**

Azithromycin, a broad-spectrum azilide, has prolonged intracellular concentrations and half-life. A large number of experimental and clinical trials done in the 1990s support its efficacy in traditional multi-drug-resistant typhoid fever.[23] However, the studies reporting the MIC of azithromycin and newer quinolones in the current scenario of ciprofloxacin-resistant enteric fever are scarce.[24] A rise in MIC over the years[23] has been attributed to irrational prescription for minor community-acquired upper respiratory, ear and sinus infections in the last decade. The misuse of azithromycin has been propelled due to its oral route of administration, as well as broad-spectrum antimicrobial activity with minimal side effects and interactions. In enteric fever, its role needs to be appreciated, as it is very effective in removing intracellular salmonellae, defervescence is rapid, gastrointestinal carriage is eradicated and, in particular, it represents a potential alternative in the pediatric population for whom quinolones are contraindicated.[22] In vitro, azithromycin has an MIC range of 4-16 μg/mL against S. Typhi. Higher clinical and bacteriological cure rate is attributable to >100-fold intracellular concentrations of azithromycin in macrophages as compared to serum.[22] The intracellular MIC may not be represented fully by currently available in vitro MIC testing methods, and such testing should be coupled with therapeutic trials. Due to its negligible relapse rate, fecal carriage, favorable outpatient compliance, azithromycin could become the preferred drug of choice over ceftriaxone, ofloxacin and chloramphenicol.[23]

Tigecycline is a glycylcycline (tetracycline analogue). It inhibits protein synthesis and evades efflux and target-mediated resistance to classical tetracyclines.In vivo and in vitro studies have demonstrated acquired

resistance associated with up-regulation of chromosomally mediated efflux pump.[25] Tigecycline lacks cross-resistance with other compounds; it could aid in therapy of pan-drug-resistant salmonelloses. Nevertheless, systematic large-scale in vivo studies are needed to assess the relative merits of tigecycline versus other drugs in these infections. Tigecycline was found to be very potent, inhibiting 97.3% of S. Typhi and all the S. Paratyphi A and ceftriaxone-resistant Salmonella isolates.[26]

The penems are a class of β-lactam antibiotics with broad-spectrum activity and are stable to hydrolysis by extended-spectrum β-lactamases-producing isolates.[25] The MIC90 for the carbapenems imipenem and meropenem in S. Typhi and S. Paratyphi A (0.064 μg/mL each) was less. Overall, faropenem had higher MIC90 at 0.25 μg/mL. Prior reports have observed faropenem to be less active than imipenem; MIC90 for was 0.5 to 1 μg/mL.[28,29]

Although the use of azithromycin, tigecycline and carbapenem is not recommended by Clinical Laboratory Standards Institute',[30] yet it may become crucial, especially in the setting of ciprofloxacin-resistant and extended-spectrum β-lactamase-producing salmonellae in enteric fever. Moreover, with increase in incidence of unusual and complicated paratyphoid fever',[29] newer broad-spectrum drugs need to be explored in the scenario of pan-drug-resistant salmonellae. Meanwhile, clinical efficacy trials are warranted to reach a definite conclusion in this regard.

# AIMS & OBJECTIVES

1) To study clinical profile of children with Enteric Fever.
2) To study Antibiotic use and outcome in children with Enteric Fever.

# REVIEW OF LITERATURE

Typhoid fever is a community-acquired systemic infection which continues to be a public health problem in developing countries. Typhoid fever is more common in resource-limited overcrowded communities with poor access to sanitation. Although the infection can occur at any age, the higher incidence in children reflects the active transmission in a community [1]Jacob john et all [1] conducted study where they searched Medline and Web of Science databases for reporting the incidence or prevalence of typhoid and paratyphoid fever confirmed by culture and/or serology, conducted in India and published between 1950 and 2015. They used binomial and Poisson mixed-effects meta-regression models to estimate prevalence and incidence from hospital and community studies, and to identify risk-factors. They identified 791 titles and abstracts, and included 37 studies of typhoid and 18 studies of paratyphoid in the systematic review and meta-analysis in their study. The estimated prevalence of laboratory-confirmed typhoid and paratyphoid among individuals with fever across all hospital studies was 9.7% (95% CI: 5.7–16.0%) and 0.9% (0.5–1.7%) respectively. There was significant heterogeneity among studies (p-values<0.001). Typhoid was more likely to be detected among clinically suspected cases or during outbreaks and showed a significant decline in prevalence over time (odds ratio for each yearly increase in study date was 0.96 (0.92–0.99) in the multivariate meta-regression model). Paratyphoid did not show any trend over time and there was no clear association with risk-factors.

The problem in the management of enteric fever is compounded by the increasing antimicrobial resistance to the first-line antibiotics used for the enteric fever.[2]The third-generation cephalosporins are presently the drug of choice for the treatment of typhoid fever. The clinical studies on efficacy are available for parenteral ceftriaxone only (not oral cefixime) and increasing MIC to ceftriaxone is a cause of concern.[3]

Sushila Dhahiya et al conducted descriptive observational study in children suffering from enteric fever as per the case definition including clinical and laboratory parameters. The antibiotic audit in hospitalized children was measured as days of therapy per 1000 patient days and in outpatient department (OPD) as antibiotic prescription on the treatment card. They concluded that out of total 128 children with enteric fever, 30 hospitalized and 98 treated from OPD, the mean duration of fever was 9.5 days at the time of presentation. Of these, 45 per cent were culture positive with *Salmonella* typhi being aetiological agent in 68 per cent followed by S. paratyphi A in 32 per cent. During hospitalization, the average length of stay was 10 days with mean duration of defervescence 6.4 days. Based on antimicrobial susceptibility ceftriaxone was given to 28 patients with mean duration of treatment being six days. An additional antibiotic was needed in six patients due to clinical non-response. In OPD, 79 patients were prescribed cefixime and additional antibiotic was needed in five during follow up visit.

They concluded that S. typhi was found to be a major etiological agent of enteric fever followed by S. paratyphi A. Ceftriaxone was prescribed as the first line in hospitalized patients while in OPD it was cefixime. However, if the patient did not show clinical improvement, another drug such as ofloxacin or azithromycin was added. The non-response to the initial antibiotic was responsible for prolonged hospitalization and increased morbidity due to increased defervescence. The delay in clinical response to ceftriaxone might be due to high MIC and required the addition of a second antibiotic in 10 per cent patients and a third antibiotic in two per cent of enrolled children.

Celina jin et al [31] conducted study to analyse response to treatment with azithromycin or ciprofloxacin, in which healthy UK volunteers (18-60 years) enrolled into two Salmonella controlled human infection studies. Study A was a single-centre, open-label, randomised trial.

Participants were randomised 1:1 to receive open-label oral ciprofloxacin or azithromycin, stratified by vaccine group (Vi-polysaccharide, Vi-conjugate or control Men-ACWY vaccine). Study B was an observational challenge/re-challenge study, where participants were randomised to challenge with Salmonella Typhi or Salmonella Paratyphi A. Outcome measures included fever clearance time, blood-culture clearance time and a composite measure of prolonged treatment response (persistent fever ≥38.0°C for ≥72 hours, persistently positive S. Typhi blood cultures for ≥72 hours, or change in antibiotic treatment). Both trials were registered with ClinicalTrials.gov (NCT02324751 and NCT02192008).

They concluded that in 81 participants diagnosed with S. Typhi in two studies, treatment with azithromycin was associated with prolonged bacteraemia (median 90.8 hours [95% CI: 65.9-93.8] vs. 20.1 hours [95% CI: 7.8-24.3], p<0.001) and prolonged fever clearance times <37.5°C (hazard ratio 2.4 [95%CI: 1.2-5.0]; p = 0.02). Results were consistent when studies were analysed independently and in a sub-group of participants with no history of vaccination or previous challenge. A prolonged treatment response was observed significantly more frequently in the azithromycin group (28/52 [54.9%]) compared with the ciprofloxacin group (1/29 [3.5%]; p<0.001). In participants treated with azithromycin, observed systemic plasma concentrations of azithromycin did not exceed the minimum inhibitory concentration (MIC), whilst predicted intracellular concentrations did exceed the MIC. In participants treated with ciprofloxacin, the observed systemic plasma concentrations and predicted intracellular concentrations of ciprofloxacin exceeded the MIC.

Their interpretation from the study was that azithromycin at a dose of 500mg daily is an effective treatment for fully sensitive strains of S. Typhi but is associated with delayed treatment response and prolonged bacteraemia when compared with ciprofloxacin within the context of a human challenge model. Whilst the cellular accumulation of

azithromycin is predicted to be sufficient to treat intracellular S. Typhi, systemic exposure may be sub-optimal for the elimination of extracellular circulating S. Typhi.

A Islam et al [32,33] did randomised controlled trial study where they compared therapeutic efficacy of ceftriaxone given once daily for 5 days vs chromaphenicolgiven four times a day for 14 days in 59 patients who were culture positive for Salmonella typhi. Ceftriaxone was given to 28 patients in once-daily intravenous doses of 75 mg/kg of body weight to children and 4 g to adults for 5 days; chloramphenicol was given to 31 patients at a dosage of 60 mg/kg/day until defervescence and then at 40 mg/kg/day to complete 14 days of treatment. All Salmonella isolates were susceptible to both antibiotics. They observed that clinical cures (defervescence without complications, no relapse, and no need for further treatment) occurred in 79% of the patients treated with ceftriaxone and 90% of those treated with chloramphenicol (P = 0.37). On the third day of treatment, blood cultures were positive for S. typhi for 60% of the patients in the chloramphenicol group and 0% of the ceftriaxone group (P = 0.001). Defervescence occurred in half the patients in both groups during the first 7 days, but on days 9 to 13 after the start of treatment, nine patients in the ceftriaxone group, compared with six patients in the chloramphenicol group, remained febrile (P=0.4). The median hematocrit and total leukocyte counts at day 14 were significantly lower for the chloramphenicol group than those for the ceftriaxone group (P = 0.01 and P = 0.02, respectively). These results indicated that the effects of therapy with ceftriaxone for typhoid fever differed from those of chloramphenicol therapy in that blood cultures became negative earlier, prolonged fever persisted in some patients, and bone marrow suppression was reduced.

It was concluded that a short, 5-day course of ceftriaxone is a useful alternative to conventional 14-day chloramphenicol therapy in the treatment of typhoid fever.

Priyanka Sharma et al [34] did study to analyse the trend in prevalence of culture-positive typhoid fever during the last decade and to determine antimicrobial susceptibility profile of Salmonella Typhi and Salmonella Paratyphi A isolated from patients of enteric fever.

All the culture-positive enteric fever cases during 2005-2016 were included in the study. Antimicrobial susceptibility was done against chloramphenicol, amoxicillin, co-trimoxazole, ciprofloxacin, ofloxacin, levofloxacin, pefloxacin, ceftriaxone and azithromycin as per corresponding CLSI guidelines for each year.

A total of 1066 strains-S. Typhi (772) and S. Paratyphi A (294) were isolated from the blood cultures during the study. A maximum number of cases were found in July-September. Antimicrobial susceptibility for chloramphenicol, amoxicillin and co-trimoxazole was found to be 87.9%, 75.5%, 87.3% for S. Typhi and 94.2%, 90.1% and 94.2% for S. Paratyphi A, respectively. Ciprofloxacin, ofloxacin and levofloxacin susceptibility were 71.3%, 70.8% and 70.9% for S. Typhi and 58.1%, 57.4% and 57.1% for S. Paratyphi A, respectively. Azithromycin susceptibility was 98.9% in S. Typhi. Although susceptibility to ceftriaxone and cefixime was 100% in our isolates, there is a continuous increase in ceftriaxone minimum inhibitory concentration $(MIC)_{50}$and $MIC_{90}$values over the time. The proportion of blood culture-positive cases during 1993-2016 ranged from a minimum of 0.0006 in 2014 to a maximum of 0.0087 in 1999.

It was concluded that the most common etiological agent of enteric fever is S. Typhi causing the majority of cases from July to October in our region. MIC to ceftriaxone in typhoidal salmonellae is creeping towards resistance and more data are needed to understand the azithromycin susceptibility.

Robert W Frenck [35]did randomised controlled study for difference between ceftriaxone and azithromycin for uncomplicated typhoid fever. During the study period, all children of 4–17 years of age who had a

clinical diagnosis of typhoid fever were included. Eligibility for enrollment required that a subject have a documented fever (temperature, ⩾38.5°C) and a history of fever for at least 4 days plus at least 2 of the following criteria: abdominal tenderness, hepatomegaly, splenomegaly, and/or rose spots.

They concluded that azithromycin given for 7 days at a dosage of 10 mg/kg/day (maximum dose, 500 mg/day) appears to be highly effective for the treatment of uncomplicated typhoid fever in children, with clinical cure rates comparable to those for ceftriaxone. Once-daily administration of oral azithromycin may offer a simple treatment regimen for typhoid fever caused by either susceptible or drug-resistant strains of *S. typhi* and may be suitable for use in areas where medical resources are limited.

Dutta et al [36]conducted a study to evaluate the role of ceftriaxone therapy in bacteriologically confirmed MDR typhoid cases who did not respond to 12-14 days of ciprofloxacin therapy. In their study a total of 140 children, aged 3-10 years, clinically diagnosed as having typhoid fever, without any clinical response after 12-14 days of ciprofloxacin therapy were screened for S. typhi by blood culture. In the bacteriologically positive children the treatment was changed to intravenous ceftriaxone for 14 days. The isolated strains of S. typhi were tested for in vitro antimicrobial susceptibility.They observed that clinical and bacteriological cure was observed with intravenous ceftriaxone therapy in all the 32 bacteriologically positive patients. All isolated S. typhi strains were uniformly (100%) susceptible to ciprofloxacin and ceftriaxone but 50 per cent of the strains were resistant to chloramphenicol. The MIC values of chloramphenicol, ciprofloxacin and ceftriaxone ranged between 125-500, 0.0625-0.5 and < 0.0625 microgram/ml respectively. It was concluded that although the S. typhi strains were susceptible to ciprofloxacin in vitro, the patients did not respond clinically and bacteriologically to ciprofloxacin therapy. Hence, ciprofloxacin may not represent a reliable and useful option for

treating MDR typhoid fever; ceftriaxone may be an effective alternative for the treatment of such cases.

During the past two decades, *Salmonella* with multiple resistance to these drugs has been reported from many countries Extended-spectrum cephalosporins and fluoroquinolones are recommended as alternatives in such a setting. However, since 1991, outbreaks or cases of infections caused by *Salmonella* resistant to extended-spectrum cephalosporins have been increasingly reported. Growing resistance to fluoroquinolones was also noted.

Lin Hui Su et all [37,38] did study where records of *Salmonella* clinical isolates from the Department of Clinical Pathology in Chang Gung Memorial Hospital (CGMH) during 1999–2003 were reviewed.

All isolates were cultured and identified by standard methods.Serogroups of the *Salmonella* isolates were determined by O antisera (Difco Laboratories, Detroit, MI, USA) using the slide agglutination method. Serotypes of ceftriaxone-resistant isolates were determined by H antisera (Difco Laboratories) using the tube agglutination method. The antimicrobial susceptibility of these isolates was investigated by a standard disc-diffusion method for non-blood isolates and by a broth-microdilution method for blood isolates.[37] The antimicrobial agents examined included ampicillin, cefixime, ceftriaxone, chloramphenicol, ciprofloxacin and trimethoprim/sulfamethoxazole. Susceptibility and resistance were defined according to the criteria suggested by the NCCL. Ceftriaxone resistance genes were amplified by PCR using consensus primer sets previously described for detecting $bla_{TEM}$, $bla_{SHV}$, $bla_{CTX\text{-}M}$ and *ampC* genes.The most important finding of this study is the emergence of ceftriaxone resistance among *Salmonella* isolates, an event also noticed in other countries. Molecular analysis indicated that the majority of ceftriaxone resistance was due to the production of CMY-2 (64%) and CTX-M-3 (27%) β-lactamases.

Several studies have been done to know the efficacy of oral cefixime vs iv ceftriaxone.

Z A Bhutta [40,41] et all in their study randomly allocated 80 children with suspected multidrug-resistant tyhpoid fever to therapy with either cefixime or ceftriaxone. Of these, an alternative diagnosis was subsequently made in 10 children and another 10 were excluded because cultures were negative. In 9 cases the typhoidal organisms isolated were susceptible to first-line drugs. In all, 50 children were randomly allocated to receive therapy with either intravenous ceftriaxone (65 mg/kg/day once daily, Group A, n = 25) or oral cefixime (10 mg/kg/day divided every 12 hours, Group B, n = 25) for 14 days. The two groups were comparable in their clinical characteristics, duration and severity of illness at the time of admission. The time to defervescence was comparable in both groups (8.3 +/- 3.7 vs. 8.0 +/- 4.1 days, P = not significant). An equal number (3 in each group) failed to respond and underwent a change in therapy. Three children in Group A and one in Group B relapsed. They concluded that oral cefixime can be used as effectively as parenterally administered ceftriaxone for management of typhoid fever in children.

Robert-Jan Hassing, Perry et al [42]took a study to investigate azithromycin susceptibility and trends in antibacterial drug resistance over time in isolates collected during 1999–2012 in the Netherlands.

During January 1999–December 2012, a total of 354 isolates were submitted by microbiology laboratories to the Salmonella National and Community Reference Laboratory under their study.All MICs were determined by using the broth microdilution method with Mueller-Hinton II cation–adjusted broth (Difco, Franklin Lakes, NJ, USA). We applied European Committee for Antimicrobial Susceptibility Testing guidelines for category interpretation for different antibacterial drugs.

They concluded that typhoidal *Salmonella* isolates in ill returned travelers from the Netherlands already showed a high percentage of increased MICs for azithromycin. Because the highest proportions of increased MICs for azithromycin was found in isolates with increased MICs for ciprofloxacin and in regions where decreased susceptibility or resistance to ciprofloxacin was already widely prevalent among *S. enterica* Typhi and Paratyphi isolates, this resistance may further limit future treatment options for enteric fever.

A study was done to look at the antibiotic susceptibility and vaccine coverage in US pediatric population by Jared McAteer et al[41] in their study out of 5131 cases of typhoid fever diagnosed and 5004 Typhi isolates were tested for antimicrobial susceptibility. Among 1992 pediatric typhoid fever patients, 1616 (81%) had traveled internationally within 30 days of illness onset, 1544 (81%) of 1906 were hospitalized (median duration, 6 days; range, 0-50), and none died. Forty percent (799) were <6 years old; 12% were <2 years old. Based on age and travel destination, 1435 (83%) of 1722 pediatric patients were vaccine-eligible; only 68 (5%) of 1361 were known to be vaccinated. Of 2003 isolates tested for antimicrobial susceptibility, 1216 (61%) were fluoroquinolone-nonsusceptible, of which 272 (22%) were also resistant to ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole (multidrug-resistant [MDR]). All were susceptible to ceftriaxone and azithromycin. MDR and fluoroquinolone-nonsusceptible isolates were more common in children than adults (16% vs 9%, P < .001, and 61% vs 54%, P < .001, respectively). Fluoroquinolone nonsusceptibility was more common among travel-associated than domestically acquired cases (70% vs 17%, P < .001). They concluded that approximately 95% of currently vaccine-eligible pediatric travelers were unvaccinated, and antimicrobial-resistant infections were common. New public health strategies are needed to improve coverage with currently licensed vaccines. Introduction of an effective pretravel typhoid vaccine for children <2 years could reduce disease burden and prevent drug-resistant infections.

Intravenous ceftriaxone is used in treatment of multi drug resistant salmonella typhi but first report of ceftriaxone resistance in *S*. Typhi was from Bangladesh in 1999.[44]Ceftriaxone resistance has remained rare, with <1% of strains resistant during 2009–2014 in Pakistan [43], and ceftriaxone continues to be the first therapeutic option for the inpatient management of typhoid. Mohammad Tahir Yousafzai et al at Aga Khan University clinical microbiology laboratory identified outbreak of ceftriaxone-resistant *Salmonella* Typhi in Hyderabad, Pakistan, through antimicrobial resistance surveillance from 30 November 2016 to 28 March 2017.The design for the investigation was a case-control study that included identification of culture-proven ceftriaxone-resistant *S*. Typhi cases, suspected cases from the households or neighborhood of the confirmed cases, and enrollment of controls matched by age to identify the risk factors. Data was collected through face-to-face interviews using a structured questionnaire. Blood cultures were obtained from all suspected cases. Drinking water samples from each household of cases and controls were obtained for microbiological testing. Geographic Information System coordinates were obtained for all cases and controls.In their case control study they could appreciate that only 2 subdistricts of Hyderabad (Latifabad and Qasimabad) were affected. A total of 101 confirmed cases of ceftriaxone-resistant *S*. Typhi had been reported in 4 months. After reporting resistance against ceftriaxone for typhoid fever, it was planned to create community awareness regarding chlorination of drinking water and sanitation measures in Hyderabad. These efforts were coordinated with the municipal water and sewage authority established to improve chlorination at processing plants and operationalize fecal sludge treatment plants. Immunization of children with typhoid conjugate vaccine within Hyderabad city was also planned.

Some studies have been done in adults for combination therapy in typhoid fever.

Niv Zmora, et al studied combination antibiotic drug therapy for typhoid as compared to monotherapy. An open-label, comparative trial was conducted at Dhulikhel Hospital, Nepal, between October 2012 and October 2014. Only culture-confirmed TF cases were eligible. Patients were alternately allocated to one of four study arms: hospitalized patients received either intravenous ceftriaxone or a combination of ceftriaxone and oral azithromycin, while outpatients received either oral azithromycin or a combination of oral azithromycin and cefexime. The primary outcome evaluated was fever clearance time and the secondary outcomes included duration of bacteremia. 105 blood culture-confirmed patients, of whom 51 were treated as outpatients, were eligible for the study. Of the 88 patients who met the inclusion criteria for FCT analysis 41 patients received a single-agent regimen, while 47 patients received a combined regimen. Results showed that fever clearance time was significantly shorter for the latter (95 versus 88 hours, respectively, p = 0·004), and this effect was exhibited in both the hospitalized and the outpatient sub-groups. Repeat blood cultures, drawn on day 3, were positive for 8/47 (17%) patients after monotherapy, versus 2/51 (4%) after combination therapy (p = 0·045). No severe complications or fatalities occurred in any of the groups. They hypothesized that the co-administration of cephalosporins and azithromycin would confer synergism due to their pharmacokinetic attributes, which suggest complimentary modes of action. While cephalosporins remain in the extracellular compartment and thereby effectively eliminate bacteremia, azithromycin readily penetrates the intracellular compartment to eradicate the pathogen in the reticuloendothelial niche.[46,47] The high efficacy of fluoroquinolones before the development of NA-resistant strains can perhaps be attributed to their excellent distribution in both the intra- and extracellular compartments.Halima Khautun et al did similar study where clinical profile, antibiotic susceptibility pattern of bacterial isolates and factors associated with complications in culture-proven typhoid patients was studied,in admitted patients in urban hospital in Bangladesh. It was retrospective analysis of clinical data from 431

patients with culture-confirmed typhoid fever admitted to Dhaka hospital of International Centre for Diarrhoeal Disease Research, Bangladesh, between January 2010 and December 2014. Clinical and microbiological profiles of the patients including age, sex, and duration of illness prior to hospital admission, haematological parameters and the antimicrobial resistance profile of the infecting isolate, duration of hospital stay and defervescence time were examined by logistic regression to identify the factors associated with complications. It was seen that about one out of three patients were children under 5 years, and 21.5% of them were severely malnourished.

Most of the patients had the common symptoms of typhoid fever such as high fever, diarrhoea and vomiting on admission while 66% cases developed diarrhoea within 1–4 days of onset of fever, which is an atypical feature in typhoid fever [50]During hospitalisation, 17.4% patients developed complications; mainly encephalopathy (6.7%), ileus (6.5%) and pneumonia (3.5%). The single fatal case in this study was an infant with severe malnutrition, pneumonia and septicemia – conditions which are identified risk factors of case fatality.[51-53] The high rate of complication in typhoid fever implies a need for early diagnosis at the community level and better management of typhoid fever.

Multidrug resistant (MDR) typhoid fever is widespread in Asian countries with evidence of the highest rate of MDR cases in Bangladesh

Ceftriaxone and cefixime remain the effective antimicrobial treatment options for this region[54,55]In this study , among culture-positive cases, 28.3% isolates showed multidrug resistant (MDR) and more than 90% of isolates were resistant to nalidixic acid and had intermediate sensitivity to ciprofloxacin. Five isolates were resistant to azithromycin but all isolates were sensitive to cefixime and ceftriaxone.

A Cochrane review suggested azithromycin to be a better antibiotic for the treatment of uncomplicated typhoid fever and as effective for MDR strains.[56] Complication was independently associated with duration of fever before admission (adjusted odds ratio: 0.85; 95% CI: 0.074–0.97; *P* < 0.05), thrombocytopenia on admission (AOR: 2.84; 95% CI: 01.06–7.57; *P* < 0.05), duration of hospital stay (AOR: 1.34; 95% CI: 1.15–1.57; *P* < 0.01) and defervescence time (AOR: 0.83; 95% CI: 0.70–0.99; *P* < 0.05).

It was concluded that high prevalence of typhoid fever among under-five children and complications among hospitalised patients are matters of concern. Sensitivity of *Salmonella* Typhi to ceftriaxone and cefixime was better than to other conventional antibiotics. Shorter duration of fever and thrombocytopenia on admission can be considered as early signs of complications.

Studies have been done for widal test as diagnostic tool for typhoid fever. Frimpong et al [55] in their study at Kumasi, Ghana screened three hundred and seven healthy food handlers and 34 blood-culture positive enteric fever patients for Salmonellae agglutinins using the Widal test. Of the 307 healthy food handlers, only 3 (1.0%) had an anti-O titre of > or = 1/160 and 8 (2.6%) an anti-H titre of > or = 1/320 for Salmonella typhi, but the majority, 214 (69.7%) and 149 (48.5%) had titres of < 1/20 for O and H agglutinins respectively. Similar agglutinin titres were also seen for S. Paratyphi A, B, and C. In the 34 enteric fever patients, for S typhi, based on anti-O titre of > or = 1/160, 25 persons showed a significant titre, a sensitivity of 73.5%, and a specificity of 99.0%. And 21 persons showed a significant titre of > or = 1/320 for anti-H, a sensitivity of 61.8% and a specificity of 97.4%. Based on these findings, titres of > or = 1/160 and > or = 1/320 for anti-0 and anti-H respectively, were considered diagnostic for enteric fever in Kumasi, Ghan.

Similar study has been done by Abraham et al [56]in Ethiopia for usefulness of a single Widal test to diagnose typhoid fever in three

study groups both retrospectively and prospectively. These were blood culture proven typhoid and non-typhoid patients and healthy individuals. Salmonella typhi H and O titres greater than or equal to 1:160 occurred in respectively 82% and 58% of typhoid fever patients; only 4% of healthy individuals and 8% of non-typhoid patients had Widal titres greater than or equal to 1:80. In typhoid fever, the H titre is elevated earlier and more frequently than the O titre. Antibody rise is maximal during the second week of illness. Antibiotic treatment did not affect the rise of antibody titre in typhoid fever. A single Widal test in an unvaccinated Ethiopian patient showing H and/or O titres greater than or equal to 1:160 and typhoid-like symptoms is strongly suggestive of typhoid fever. It also appears that H titre is more useful than O titre. More false positives are found than false negatives. Under these circumstances, the clinical picture is the decisive factor in making a diagnosis of typhoid.

# MATERIAL METHODS

## SOURCE OF DATA

This descriptive prospective study was conducted in the departments of Paediatrics and Microbiology,Dayanand Medical College and Hospital,Ludhiana,Punjab,India and all in patients who are either confirmed cases or probable cases of Enteric Fever irrespective of the age of children,admitted under the Pediatric departments in DMCH from month of February 2020 to month of August 2021 were included for studying clinical profile and antibiotic use.

**Inclusion Criteria**: All patients with a diagnosis of Enteric fever as per the case definition as described below after informed written consent were included in the study.

**Case definitions**: This was based on Paediatric department, DMCH, Ludhiana, protocols adapted from the WHO and Indian Academy of Paediatrics (IAP) guidelines.

**Confirmed case**: A patient with fever (38°C and above) that has lasted for at least three days, with a laboratory-confirmed positive culture (blood, bone marrow and bowel fluid) of Salmonella Typhi or S. Paratyphi A.

**Probable case:** A patient with fever (38°C and above) that has lasted for at least three days, with a clinically consistent case with positive serodiagnosis but without S. Typhi and S .Parattyphi isolation.

**Exclusion Criteria**: Those inpatients who did not meet case definition of Enteric Fever and those who did not give consent were excluded.

**Collection of Data**: Based on the pre-defined proforma, patient's demographic and clinical details were recorded

**Blood Cultures**: Under all aseptic precautions,10 – 20 ml of blood withdrawn from antecubital vein with disposable syringe and inoculated

directly into commercially prepared BACTEC 9240 or Bact /Alert culture bottles.

**Sample Processing**: Samples received in microbiology lab were processed as per standard protocols.

Blood specimenwereprocessed in the Bactec or Bact -T / Alert microbial detection system. The blood culture bottles were loaded in the instrument and incubated for a maximum period of 7 days or till the bottle indicates positive by the system and time to show positive were noted.

Bottles were placed into receiving wells that were monitored once every 10minutes.

If the voltage change exceed a present delta value, the microcomputer flagged the bottle as positive.

Processing of blood culture positive bottles:

Smears were prepared from the positive blood culture bottles and gram staining of the smears was done.

Also the positive bottles were subcultured on blood agar and MacConkey agar plate. The plate was incubated at 37 degrees centigrade for 18 – 24 hours.

Antibiotic sensitivity testing was done of Salmonella isolates for antibiotics And MIC was calculated.

Sensitivity against these antibiotics will be observed.
Azithromycin
Ceftriaxone
Cefixime
Cefuroxime
Ciprofloxacin
Ofloxacin

Ampicillin
Chloramphenicol
Cotrimoxazole

**Serodiagnosis by Widal Test**

The Widal test reaction involves the use of bacterial suspensions of S typhi and S paratyphi ‘A’ and ‘B’, treated to retain only the ‘O’ and ‘H’ antigens. These antigens were employed to detect corresponding antibodies in the serum of a patient suspected of having typhoid fever. The IgM somatic O antibody appeared first and represented the initial serologic response in acute typhoid fever, while theIgG flagella H antibody developed more slowly but persisted for longer.

The result of the tests were scored from 0 to 4+, ie, 0 (no agglutination), 1+ (25% agglutination), 2+ (50% agglutination), 3+ (75% agglutination) or 4+ (100% agglutination). The smallest quantity of serum that exhibited a2+ or 50% agglutination was considered the end-point of serum activity or titre.

The tube agglutination test required much more technical work than the rapid slide test, and was macroscopic test. It also served as a means of confirming the results of the slide test. A mixture of suspended antigen and antibody was incubated for up to 20 h at 37°C in a water bath. Agglutinations were visualised in the form of pellets, clumped together at the bottom of the test tube. Results were scored from 0 to 4+ positive agglutination as described above for the slide test. The tube test was useful to clarify erratic or equivocal agglutination reactions obtained by the more rapid slide test.

In this descriptive study

**Demographic Variables** included
Gender distribution
Age Group

**Clinical Profile of Enteric Fever included**

**Fever Characteristics**

**Associated Symptoms**

Rigors, Chills

Pain Abdomen

Loose stools, Vomitings

Abnormal Body movements

**Past History Of Antibiotic Intake**

Type of antibiotic intake, Duration of antibiotic intake

**Vaccination History**

**Physical Examination**

Anemia, Icterus, Edema, Hepatosplenomegaly, Hepatomegaly

**Laboratory Investigations** done were

Hemogram

Inflammatory markers

**Serodiagnosis**

Widal Test

**Gold Standard** taken was

Blood Culture

**Antibiotic sensitivity profile** was studied and drug resistance comparison between Salmonella Typhi and Paratyphi was done and multi drug resistance was also studied

By taking this clinical profile and drug sensitivity into consideration, Antibiotics were used in enrolled patients and effect on day of defervescence of fever, duration of hospital stay and outcome was studied.

## OUTCOME

In all 70 enrolled patients, clinical profile of Enteric Fever was studied, antibiotics were given as per antibiotic sensitivity profile and all patients were discharged.

## NUMBER OF CASES

Total number of cases = 70

61 cases were Confirmed cases based on blood culture and 9 cases were probable cases with clinical profile and serodiagnosis widal test.

## STATISTICAL ANALYSIS

Data were described in terms of range; mean ±standard deviation (± SD), frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical prog

# OBSERVATIONS & RESULTS

Demographic Variables

**Gender Distributions**

Out of all 70 patients enrolled, 28 cases 40% patients were female and 42 cases, 60 % were male.

**Table1: Gender Distributions**

| Gender | No. of cases | Percentage |
|---|---|---|
| female | 28 | 40 |
| male | 42 | 60 |
| Total | 70 | 100.0 |

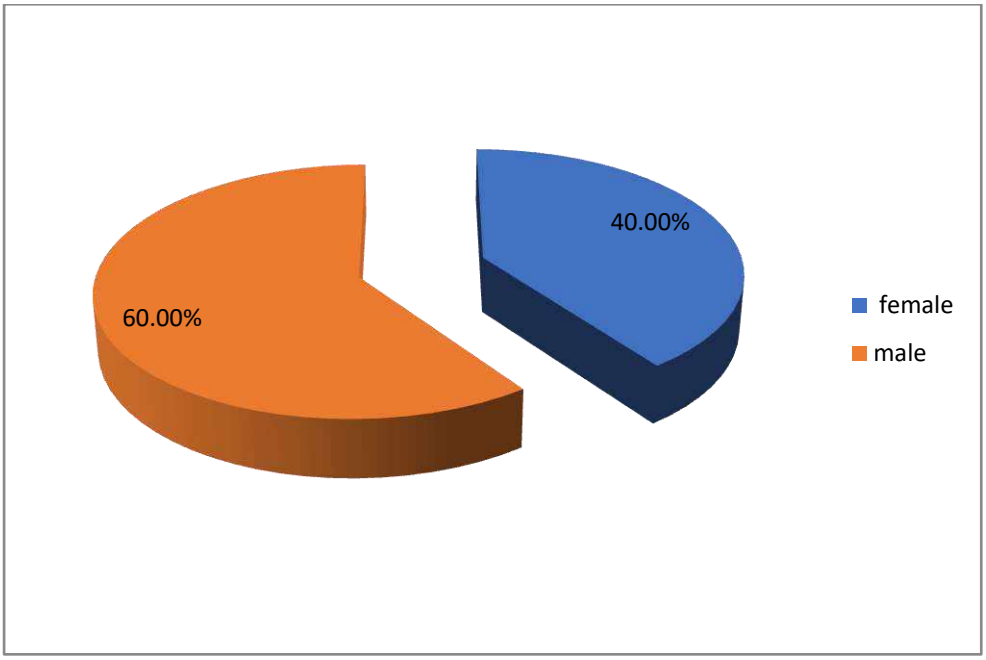



**Figure 1:Gender Distributions**

**Age Group**

70 enrolled patients

7 cases were in age group less than equal to 12 months of age, 30 cases were in age group of 12 months to 60 months and 37 were in age group more than 60 months.

With mean age 76.5 months.with SD 52.68.

**Table 2: Age Group Distribution**

| Age group | No. of cases | Percentage |
|---|---|---|
| < 12 | 18 | 25.7% |
| >12<60 | 19 | 27.2% |
| > 60 | 33 | 47.1% |
| Total | 70 | 100.00% |

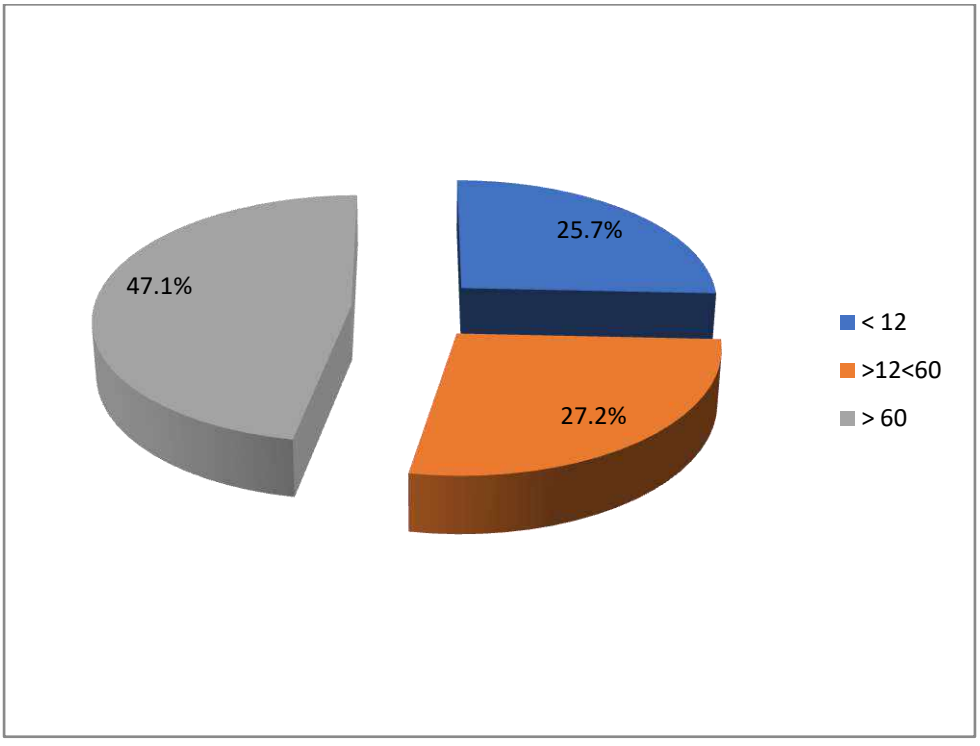



**Figure 2: Age Group Distribution**

All cases had **Fever** at admission

**Onset of Fever**

62 casesmaking 88.6 % of total had acute onset fever 8 cases, 11.4 % had insidious onset fever.

**Table 3: Onset Of Fever**

| Onset Of Fever | No. of cases | Percentage |
|---|---|---|
| acute | 62 | 88.6% |
| insidious | 8 | 11.4% |
| Total | 70 | 100.0% |

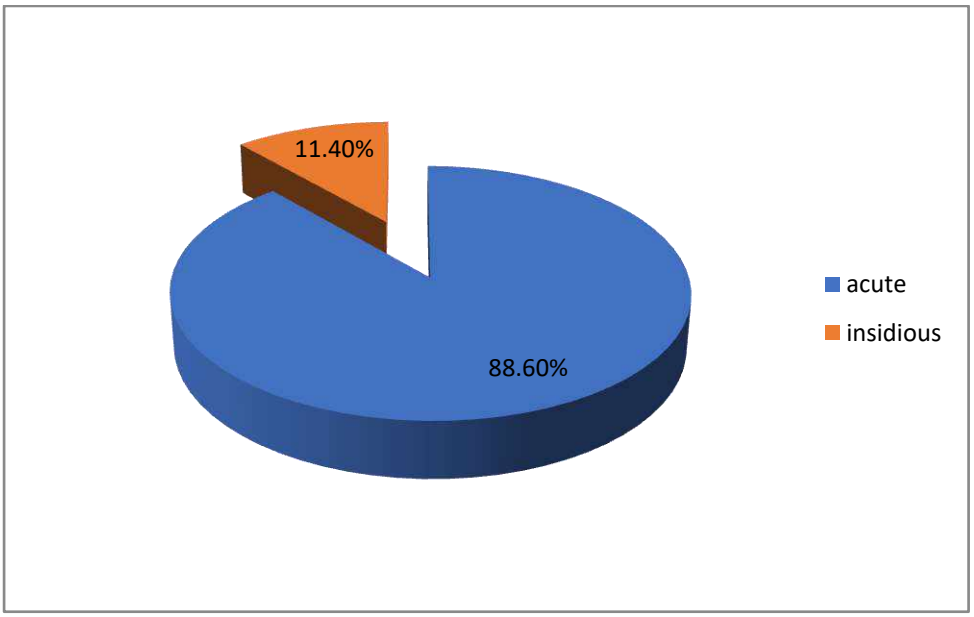



**Figure 3: Onset Of Fever**

**Grade of fever**

33 of total cases, making 47.1 % cases had high grade fever 37 cases, accounting for 52.9 % of total had moderate grade of fever.

**Table 4: Grade of fever**

| Grade Of Fever | No. of cases | Percentage |
|---|---|---|
| high | 33 | 47.1% |
| moderate | 37 | 52.9% |
| Total | 70 | 100.0% |

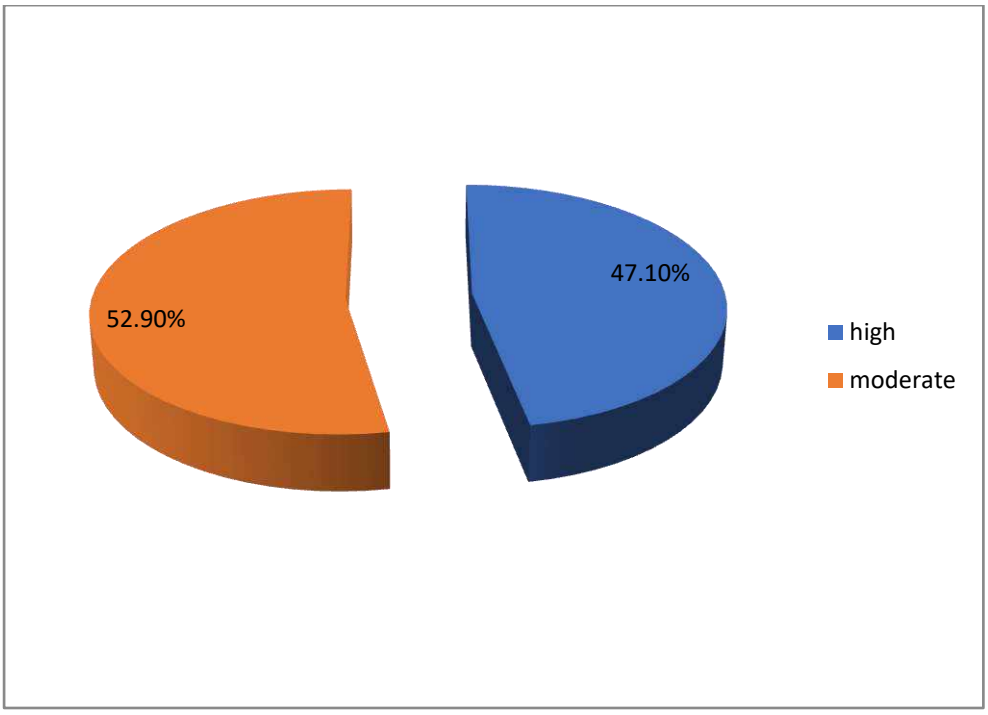



**Figure 4: Grade of fever**

All cases had intermittent fever

**Association with Rigors Chills**

59 cases making 84.3 % of total had no chills and rigors and11 cases, 15.7 % had chills and rigors at admission.

**Table 5: Number of cases with Chills rigors**

| Rigors/Chill | No. of cases | Percentage |
|---|---|---|
| not present | 59 | 84.3% |
| present | 11 | 15.7% |
| Total | 70 | 100.0% |

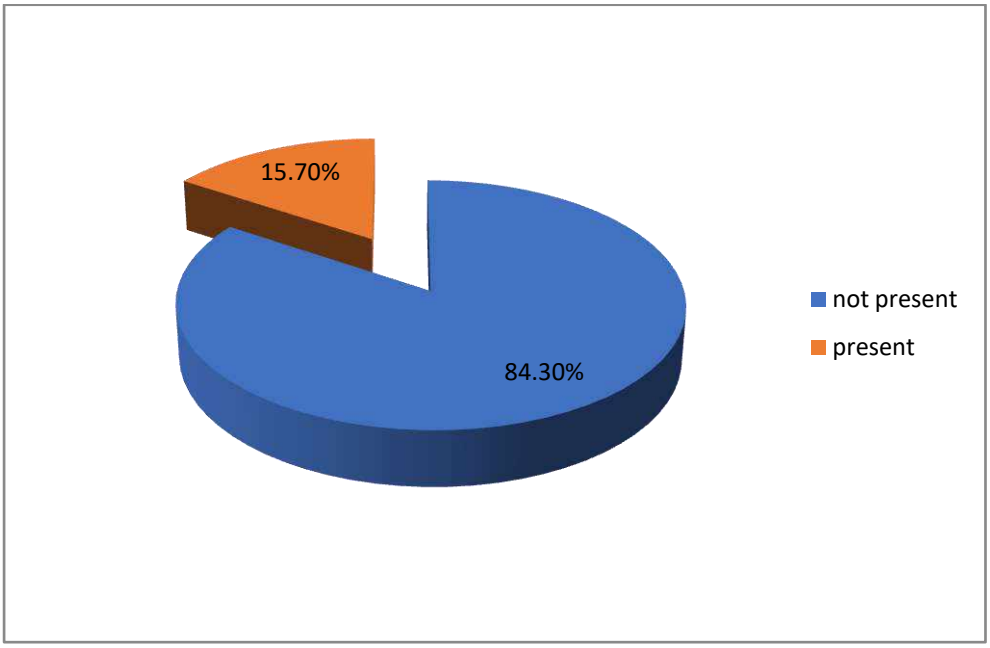



**Figure 5:Number of cases with Chills rigors**

**Associated Symptoms**

**Pain abdomen**

48 cases, 68.6 % of total, had no pain abdomen at admission

22 cases, 31.4 % of total, had pain abdomen at admission.

**Table 6:Number of cases with Pain Abdomen**

| Pain Abdomen | No. of cases | Percentage |
|---|---|---|
| not present | 48 | 68.6% |
| present | 22 | 31.4% |
| Total | 70 | 100.0% |

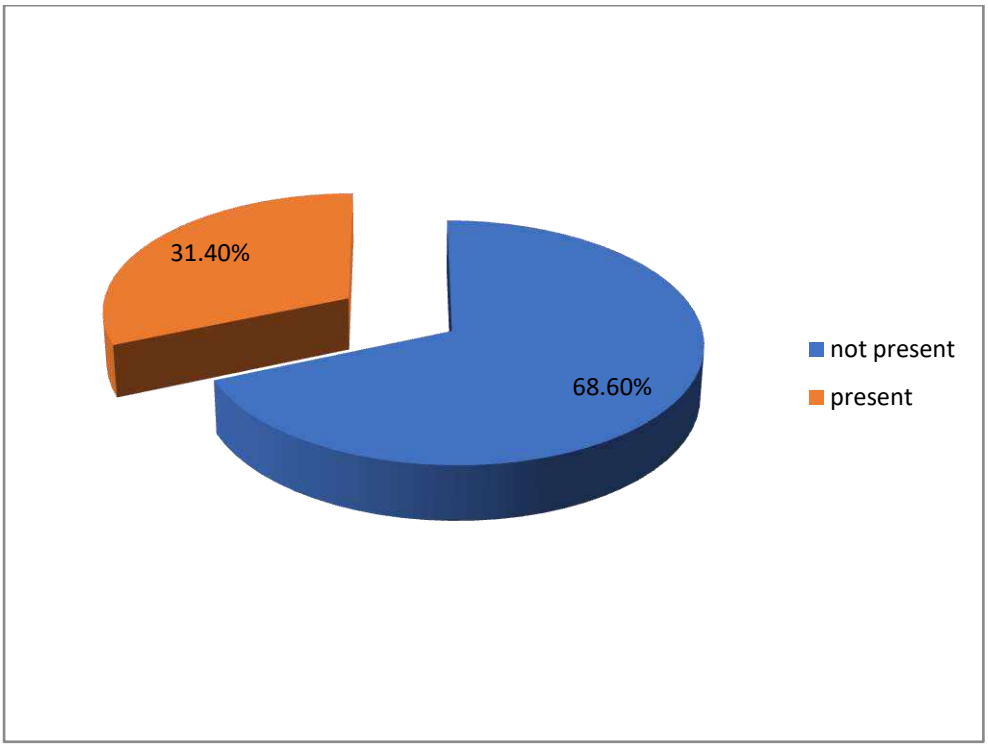



**Figure 6:Number of cases with Pain Abdomen**

**Table 7: Duration of Pain abdomen**

| Pain abdomen | No. of cases | Percentage |
|---|---|---|
| Duration | 22 | 31.4% |
| < 3DAYS | 18 | 25.7% |
| 3-7 DAYS | 4 | 5.7% |

All cases with pain abdomen had mild pain

18 cases, 25.7 % had duration <3 days

4 cases, 5.7 % of total had duration between 3 to 7 days .

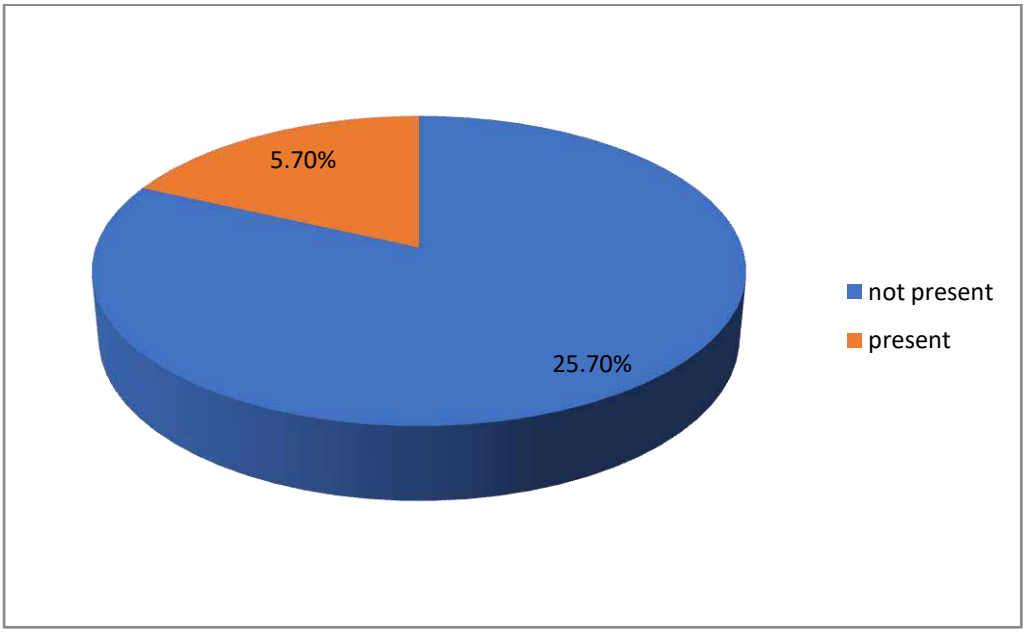



**Figure 7: Duration of Pain abdomen**

**Table 8: Number of cases with Loose Stools and Vomitings**

| Loose Stools / Vomitings | No. of cases | Percentage |
|---|---|---|
| not present | 35 | 50.0% |
| present | 35 | 50.0% |
| Total | 70 | 100.0% |

50 % of patients had associated loose stools and vomitings.

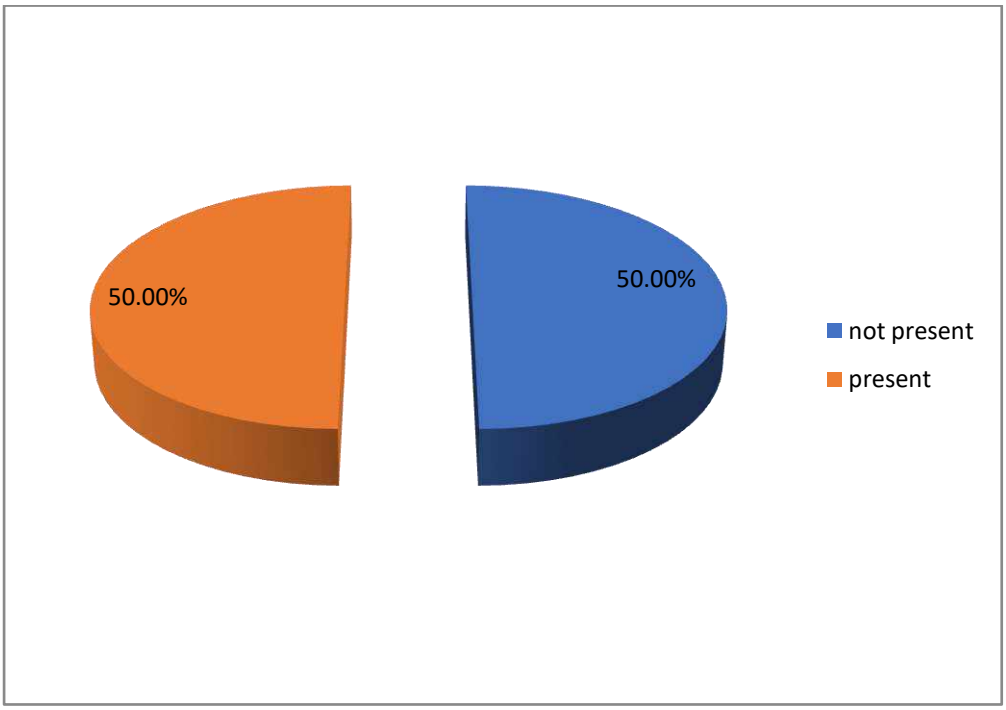



**Figure8:Number of cases with Loose Stools and Vomitings**

**Table 9: Duration of Loose Stools and Vomitings**

| Loose stools / Vomitings duration | No. of cases | Percentage |
|---|---|---|
| < 3DAYS | 14 | 20.0% |
| 3-7 DAYS | 21 | 30.0% |

In 14 cases, 20 % of total,had duration <3 days

In 21 cases, 30 % of total, duration was 3 – 7 days.

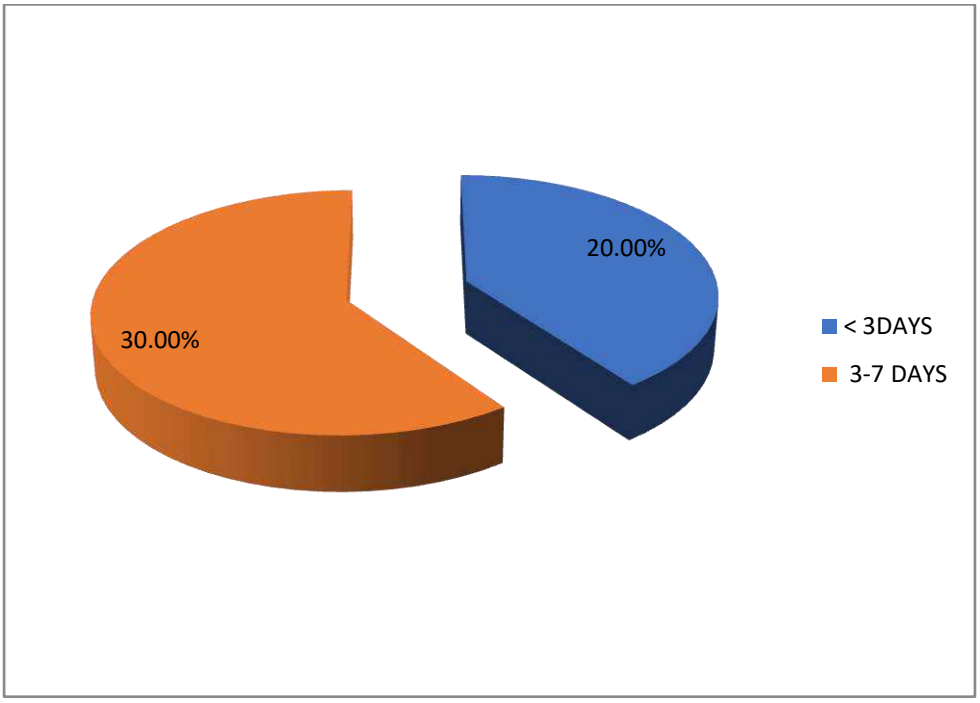



**Figure 9: Duration of Loose Stools and Vomitings**

**Abnormal Body Movements**

5 cases, 4.2 % of total had abnormal body movements

65 cases, 92.9 % had no abnormal body movements

**Past History of Antibiotic Intake**

1 patient, 1.4 % of total had received iv antibiotic, i/v vancomycin and iv ceftriaxone,before hospitalization

1 patient, 1.4 % of total had received, iv and oral medication i/v amikacin and oral azee

18 cases, 25.7 % had taken oral medication

**Table 10: Number of cases with Past History of Antibiotic Intake**

| Past Drug History | No. of cases | Percentage |
|---|---|---|
| IV | 1 | 1.4% |
| iv+oral | 1 | 1.4% |
| oral | 18 | 25.7% |

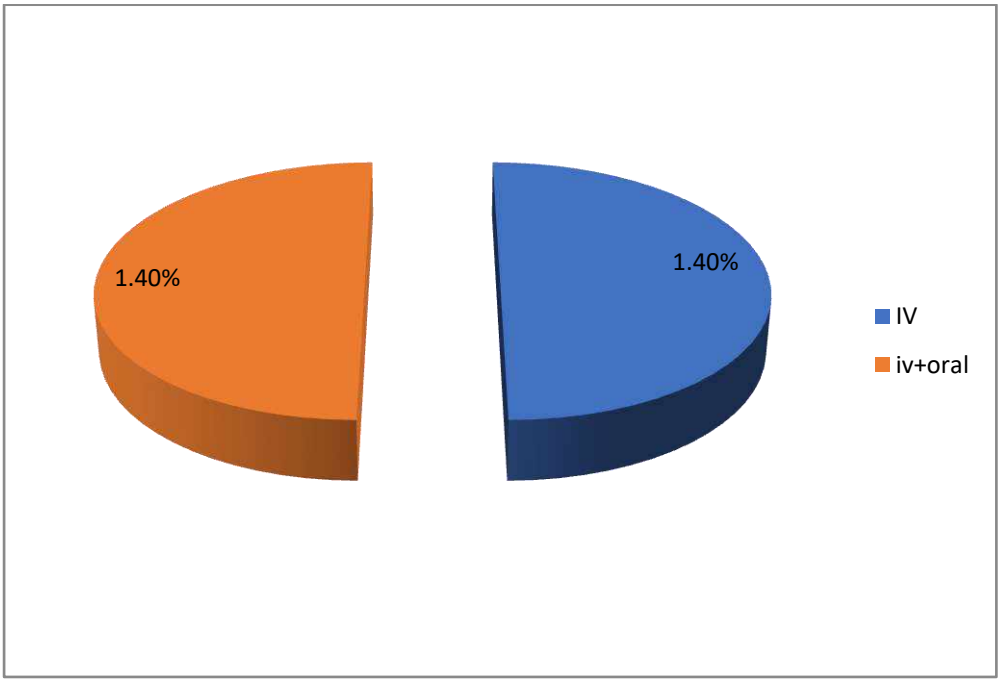
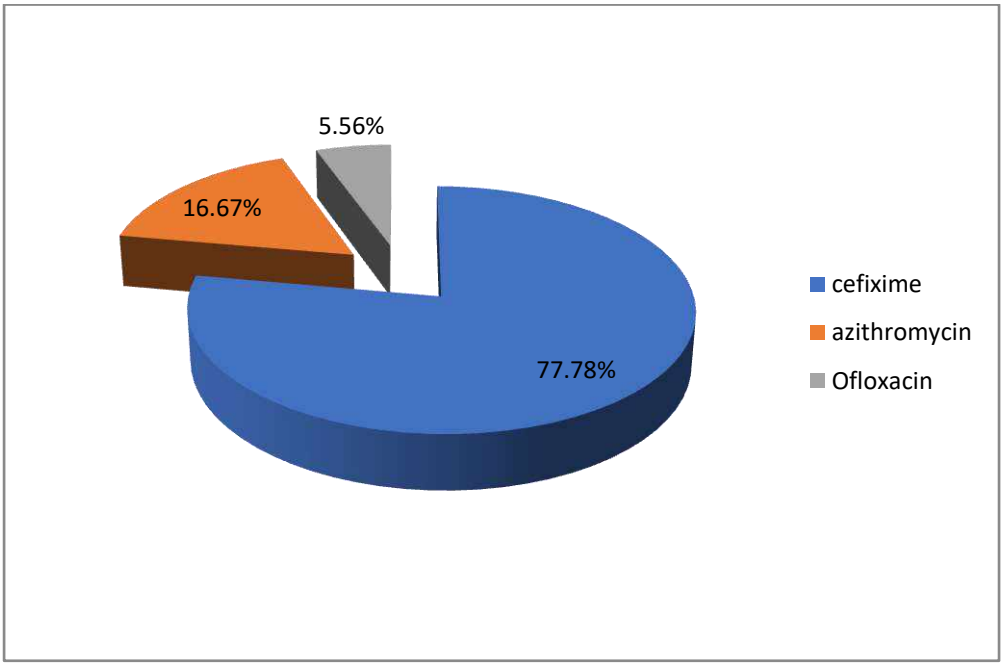



**Figure10: Number of cases with Past History of Antibiotic Intake**

**Figure 11: Number of cases with history of oral antibiotic intake**




Type Of oral antibiotic

14 cases had received oral cefixime

1 patient had received ofloxacin

3 patients had azithromycin intake .

**Table 11: Type of Antibiotic taken**

| Type of Antibiotic taken | No. of cases | Percentage |
|---|---|---|
| Azee | 3 | 15.00% |
| cefixime | 14 | 70.00% |
| inj Amikacin , Oral Azee | 1 | 5.00% |
| inj Vancomycin and inj . ceftriaxone | 1 | 5.00% |
| Ofloxacin | 1 | 5.00% |
| Total | 20 | 100.00% |

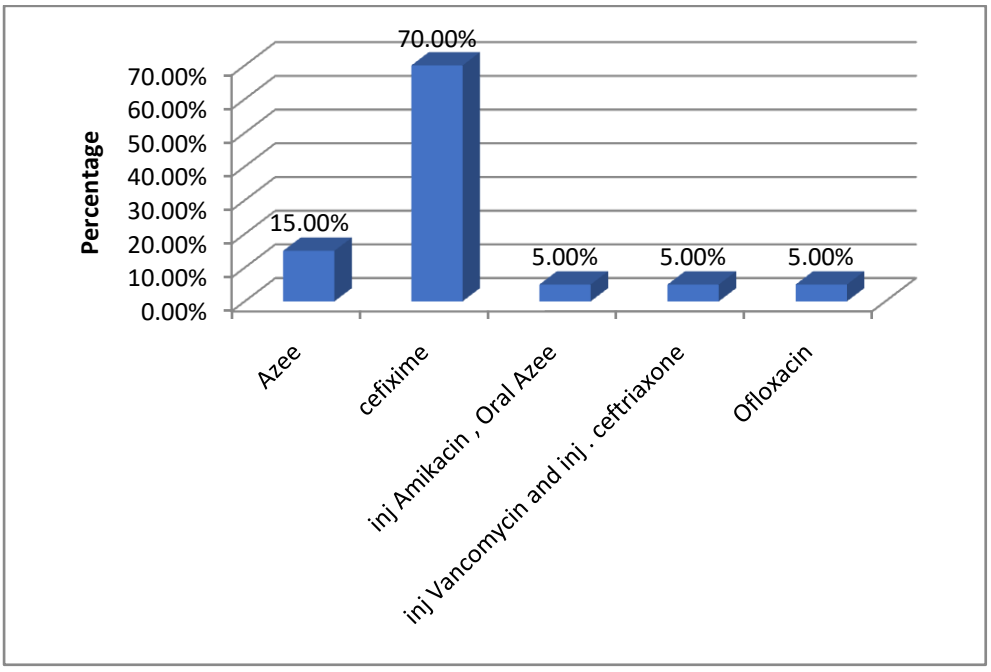



**Figure12: Type of Antibiotic taken**

**Duration of Antibiotic intake**

Of total 20 cases, who received antibiotics, 9 cases making 45% of total had taken antibiotics for 2 days, followed by 3 cases making 15 % of total, had taken antibiotics for 5 days before hospitalization.

**Vaccination History**

Only one case making 1.4 % of total had received conjugate vaccine against 69 cases, 98.6 % total unimmunized patients.

**Table 12: Number of cases with Vaccination History**

| Vaccination History | No. of cases | Percentage |
|---|---|---|
| 1 dose of typhoid vaccine, conjugated typhoid vaccine. | 1 | 1.4% |
| Not vaccinated for typhoid | 69 | 98.6% |
| Total | 70 | 100.0% |

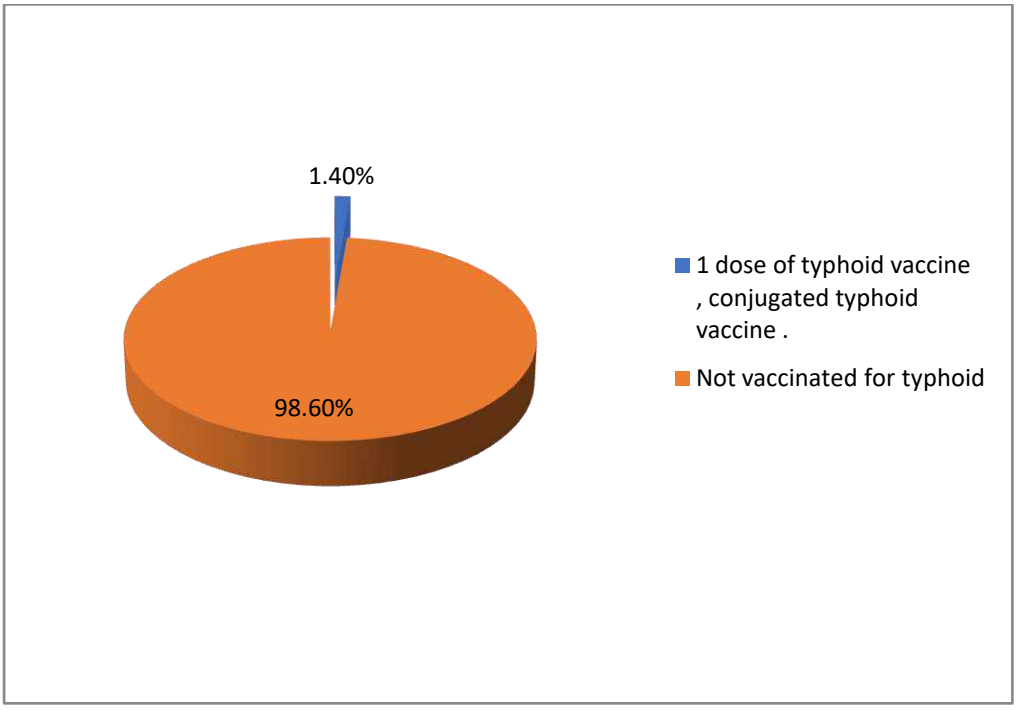



**Figure13: Number of cases with Vaccination History**

**Hospital Stay**

Of total 70 patients admitted, 17 cases, 24.3 % of total had hospital stay of 8 days, followed by 13 cases , 18.6 % of total with hospital stay of 5 days . Mean duration of hospital stay 7.37 days with SD 2.71

**Table 13: Duration of Hospital Stay**

| Hospital stay ( days ) | No. of cases | Percentage |
|---|---|---|
| 1 | 2 | 2.9% |
| 3 | 2 | 2.9% |
| 4 | 3 | 4.3% |
| 5 | 13 | 18.6% |
| 6 | 4 | 5.7% |
| 7 | 10 | 14.3% |
| 8 | 17 | 24.3% |
| 9 | 7 | 10.0% |
| 10 | 3 | 4.3% |
| 11 | 6 | 8.6% |
| 12 | 1 | 1.4% |
| 13 | 1 | 1.4% |
| 17 | 1 | 1.4% |
| Total | 70 | 100.0% |

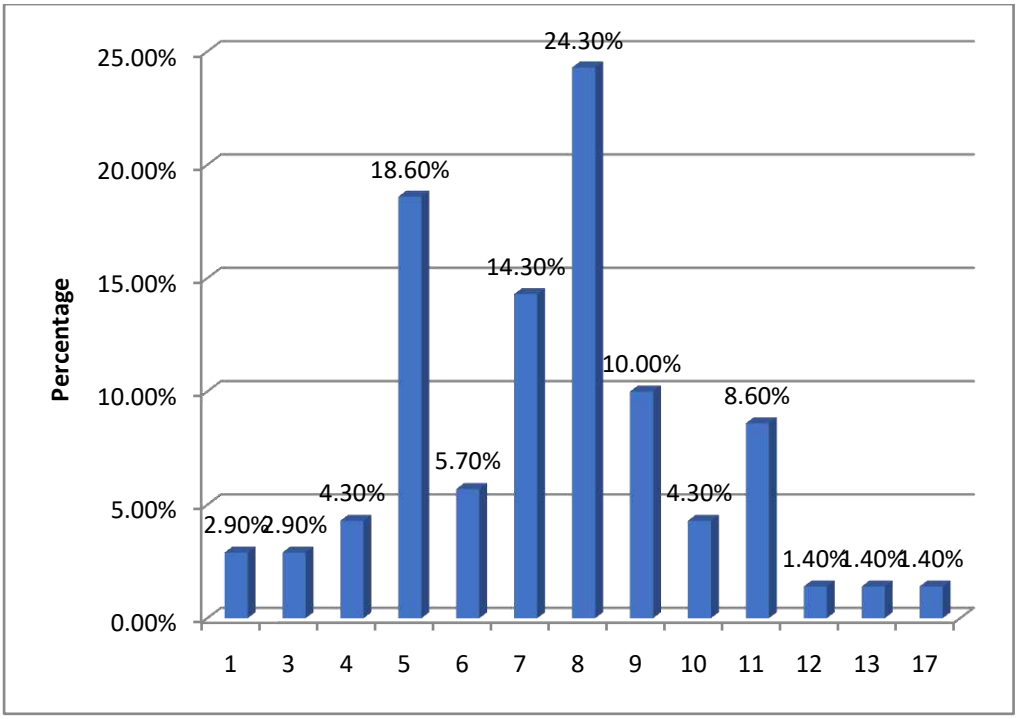



**Figure 14: Duration of Hospital Stay**

**On Examination**

**Anemia**

Anemia was common sign in enteric fever patients, in our study, 68 cases making 97.1 % of total had pallor.

2 cases, making 2.9 % of total, didn't have pallor at admission.

Most cases , 39 , 57.4 % of total had mild anemia , 24 cases , 35.3 % cases of total had moderate anemia and 5 cases , 7.4 % of total had severe anemia.

**Table 14: Number of cases with Anemia**

| Anemia | No. of cases | Percentage |
|---|---|---|
| Mild | 39 | 57.4% |
| moderate | 24 | 35.3% |
| severe | 5 | 7.4% |
| Total | 68 | 100.0% |

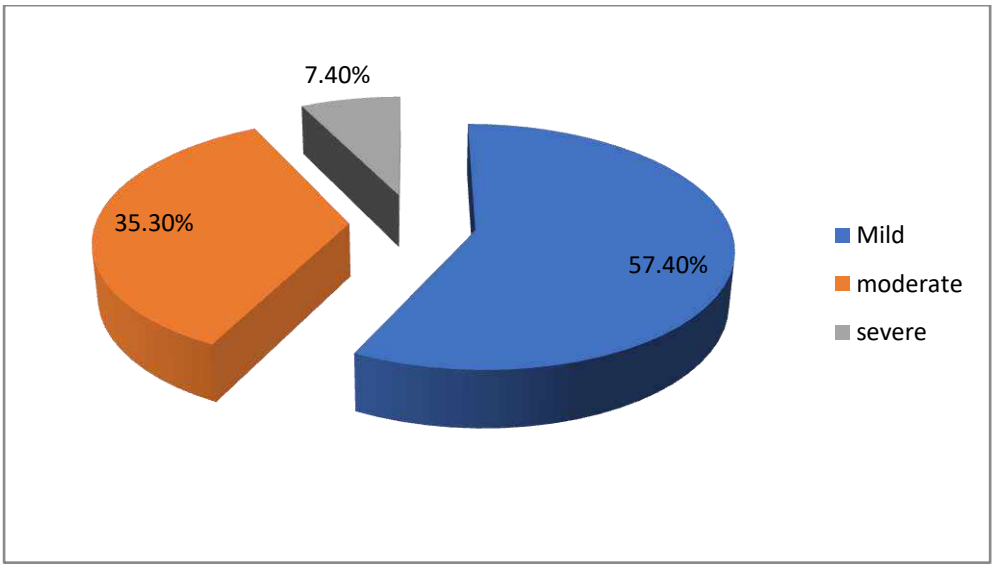



**Figure15: Number of cases with Anemia**

**Icterus**

No case had icterus at admission.

**Edema**

We also have seen edema in only 1 patient, making 1.4 % of total, whereas, 98.6 % cases had no edema

**Hepatosplenomegaly& Hepatomegaly**

Hepatosplenomegaly was noticed in 18 patients, 25.7% cases

Whereas hepatomegaly was found in 33 cases, 47% of total splenomegaly was not found in any case.

**Table 15: Number of cases with Hepatosplenomegaly & Hepatomegaly**

| | **No. of cases** | **Percentage** |
|---|---|---|
| Hepatosplenomegaly | 18 | 25.7% |
| hepatomegaly | 33 | 47.1% |
| splenomegaly | 0 | 0.0% |

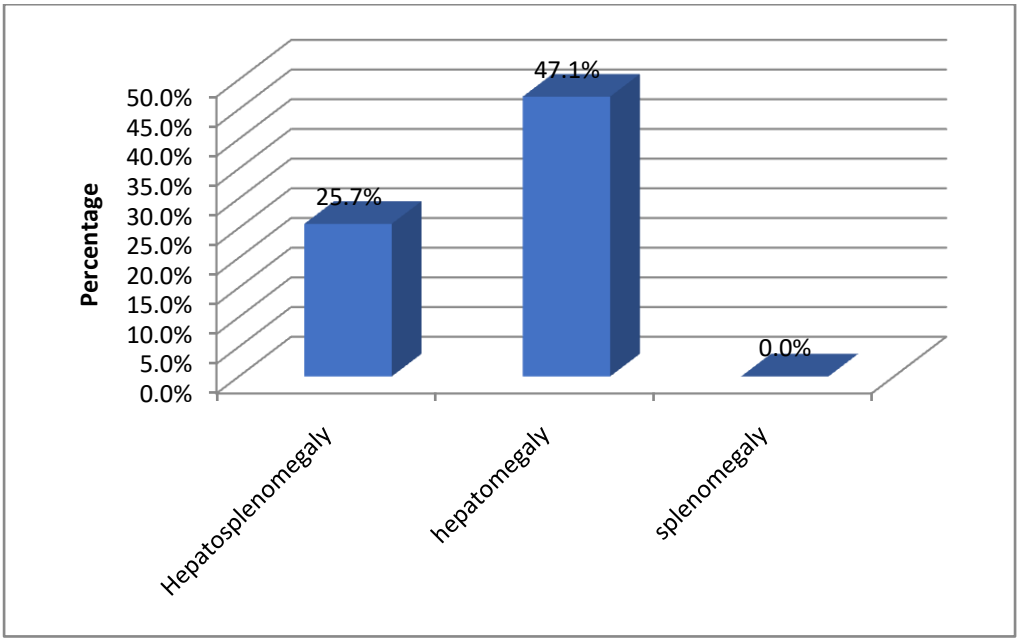



**Figure16: Number of cases with Hepatosplenomegaly & Hepatomegaly**

**Laboratory Investigations**

**Hemogram**

Hemogram was tested in all 70 cases, Minimum Hemoglobin found is 5.1 gm%, maximum being 13.8 gm % with mean value of 10.10. SD 2.09.

Minimum MCV observed is 18.9, maximum being 186 with mean value of 61.1 and SD 26.2

Leucocytosis has been seen in most cases with mean value of 10961, minimum TLC seen is 6700, maximum being 97000. SD 16340

Eosinopenia has been seen in our cases, with minimum Eosinophil count of 0.0, maximum being 14 with mean value of 0.43 and SD 1.71

Minimum platelet count which is seen is 12000, maximum being 295000

**Inflammatory markers**

**CRPq**

CRPq is tested in 66 patients, is considered positive if value more than 6 mg%, Found to be positive in 64 cases , 96.9 % of total , with maximum value of 234.3,And negative in 2 cases, 3% of total tested, with minimum value of 0.96

Mean value seen is 71.3 with SD of 48.3

**ESR,** Erythrocyte Sedimentation Rate

ESR is tested in 15 cases, minimum value being 2.0, maximum of 120 and mean being 36.13 with SD 30.89

**LDH**

Normal range being kept is 135 – 225 , It is tested in 48 patients , came out to normal in 1 case out of 48 tested , and positive in rest 47 cases . minimum value being 224 , maximum value of 1355 with mean value of 550.9 and SD of 247.3

**SGOT**

SGOT also known as serum glutamic oxaloacetic transaminase,

Is done in 52 cases , normal value kept between 0 – 40 U /L , came out to be normal in 3 cases , minimum value being 22 , maximum being 374 , with mean value of 109.7 with SD of 76.9

**SGPT**

SGPT also known as Serum Glutamic pyruvic transaminases, normal value kept between 0 – 40 Units.

It was tested in 53 cases, came out to be normal in 13 cases making. Minimum value being 20, maximum 843 and average of 89.6 with SD value of 115.4

**Table 16: Number of cases with raised inflammatory markers.**

| | Number of cases | Raised | Mean value | Percentage |
|---|---|---|---|---|
| CRP | 66 | 64 | 71.3 | 96.90% |
| ESR | 15 | 12 | 36.13 | 80.00% |
| SGOT | 52 | 49 | 109.79 | 94.23% |
| SGPT | 53 | 40 | 89.68 | 75.47% |
| LDH | 48 | 47 | 550.9 | 97.92% |

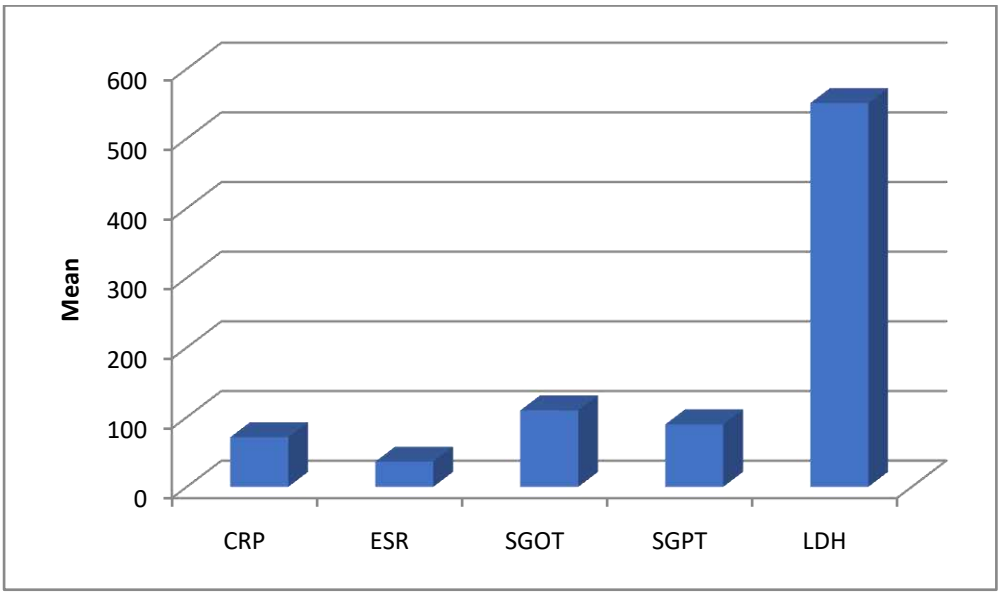



**Figure17: Mean number of cases with raised inflammatory markers.**

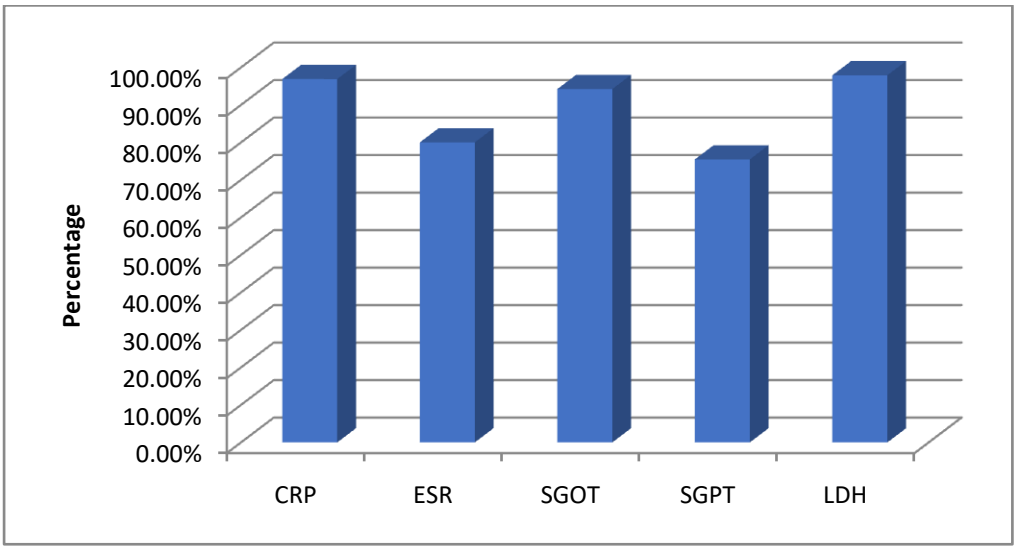



**Figure18: Percentage of number of cases with raised inflammatory markers.**

**Serodiagnosis**

**Widal Test:**

**Table 17: Number of cases of widal test**

| | No. of cases | Percentage |
|---|---|---|
| TO+TH | 24 | 61.50% |
| TO+AH | 5 | 12.80% |
| TO | 4 | 10.20% |
| NEGATIVE | 6 | 15.30% |

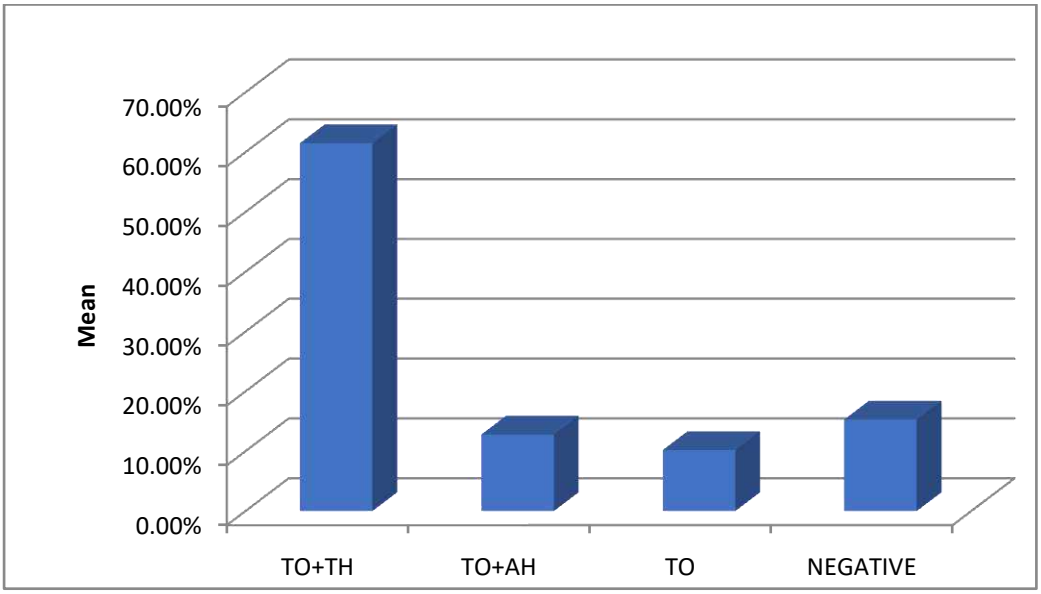



**Figure19: Number of cases of widal test**

**Widal test** is done in 39 cases out to total 70 cases. TO titers of more than 80 are considered significant and TH titers of more than 160 are considered significant.

TO and TH titers depict growth of Salmonella typhi, which came out to be positive in 24 cases making 61.5% of total.

TO and AH, depicting growth of salmonella paratyphi, came out to be positive in 5 cases, 10.2 % of total.

Alone TO titers, more than 160, is considered significant and depict Enteric Fever .which is found in 4 cases, making 10.2 % of total.

Widal test came out to be negative in 6 cases, 15.3 % of total.

**Table 18: Number of cases with titers of widal test**

| Titers | NEGATIVE | TO | TO+AH | TO+TH | Total |
|---|---|---|---|---|---|
| 20 | 2 | 0 | 0 | 0 | 2 |
| 40 | 4 | 0 | 0 | 0 | 4 |
| 80 | 0 | 0 | 0 | 0 | 0 |
| 160 | 0 | 1 | 1 | 5 | 7 |
| 320 | 0 | 3 | 3 | 11 | 16 |
| 640 | 0 | 0 | 1 | 2 | 3 |
| 2560 | 0 | 0 | 0 | 5 | 6 |
| 1260 | 0 | 0 | 0 | 1 | 1 |
| Total | 6 | 4 | 5 | 24 | 39 |

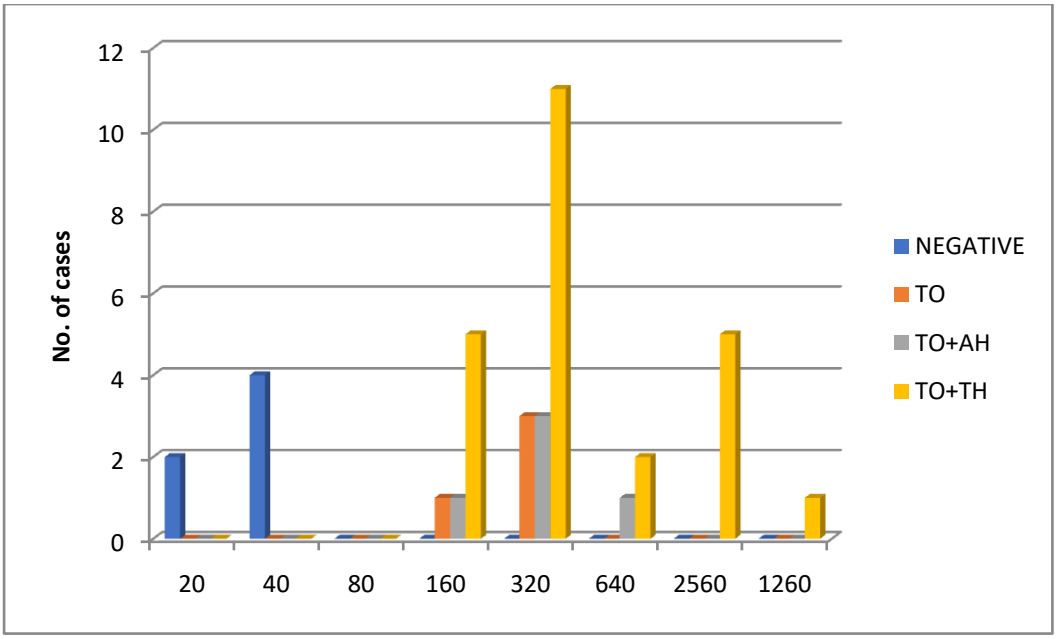



**Figure 20: Number of cases with titers of widal test**

Out of total 24 positive Widal titers for Typhoid Fever , 5 cases had titers of 1:160 , 11 , maximum number of cases , had titers of 1:320 , 2 cases with titers of 1:640 , 1 case with titers 1:1260 and 5 with titers of 1: 2560 .

Of total 5 positive Widal titers for Paratyphoid Fever, 1 case had titers of 1:160, 3 cases with titers of 1:320 and 1 case with titers of 1:640.

Of total 4 positive titers for TO, 1 case had titers of 1:160 and 3 cases with titers of 1:320.

Of all 6 cases with negative Widal test , 2 fall in category with titers of 1:20 , 4 cases with 1 : 40 .

**Blood Culture**

**Table 19: Number of cases with blood culture**

| Blood Culture | No. of cases | Percentage |
|---|---|---|
| Salmonella Typhi | 52 | 74.30% |
| Salmonella ParayphiA | 9 | 12.90% |
| no growth | 9 | 12.90% |
| Total | 70 | 100.00% |

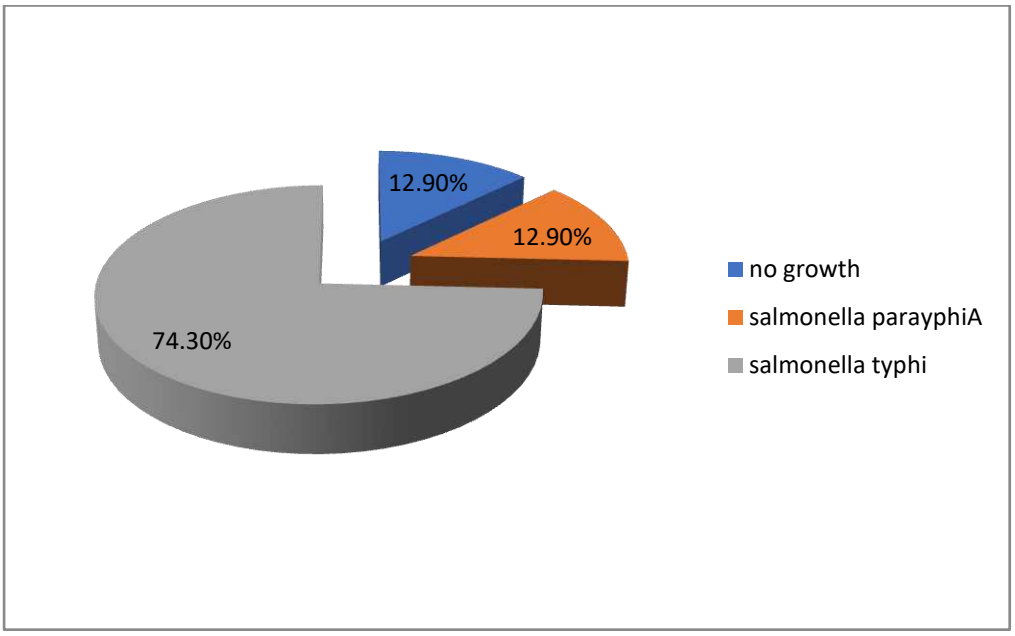



**Figure21: Number of cases with blood culture**

Total 70 cases were enrolled, out of which, 61 cases had blood culture positive.

52 cases with blood culture growth of Salmonella Typhi and 9 cases with blood culture growth of Salmonella Paratyphi

**Table 20: Antibiotic Sensitivity Profile of Salmonella Typhi Isolates**

| | salmonella typhi | |
|---|---|---|
| | **Number of isolates** | **Percentage** |
| Azithromycin | 52 | 100.00% |
| cotrimoxazole | 52 | 100.00% |
| Cefixime | 48 | 92.31% |
| Cefuroxime | 2 | 3.85% |
| Ceftriaxone | 52 | 100.00% |
| Ciprofloxacin | 1 | 1.92% |
| Ofloxacin | 42 | 80.77% |
| Ampicillin | 50 | 96.15% |
| Chloramphenicol | 50 | 96.15% |

Sensitivity profile has been studied for Samonella Typhi Isolates and it has been seen that **Azithromycin** is sensitive in all culture growths of Salmonella Typhi with sensitivity of 100 %.

**Cotrimoxazole** is sensitive in all isolates.

Sensitivity of **Cephalosporins**

Ceftriaxone has maximum sensitivity of 100 percent followed by Cefixime with sensitivity of 92.3 percent and least sensitivity of cefuroxime with sensitivity in 3.85% cases only.

**Chloramphenicol** has sensitivity in 96.1 % cases

In **Quinolone** group Ofloxacin is found to be sensitive in 80.7% cases whereas Ciprofloxacin being sensitive in 1.9 % cases only.

**Ampicillin** is sensitive in 50 cases making 96.1% of total cases.

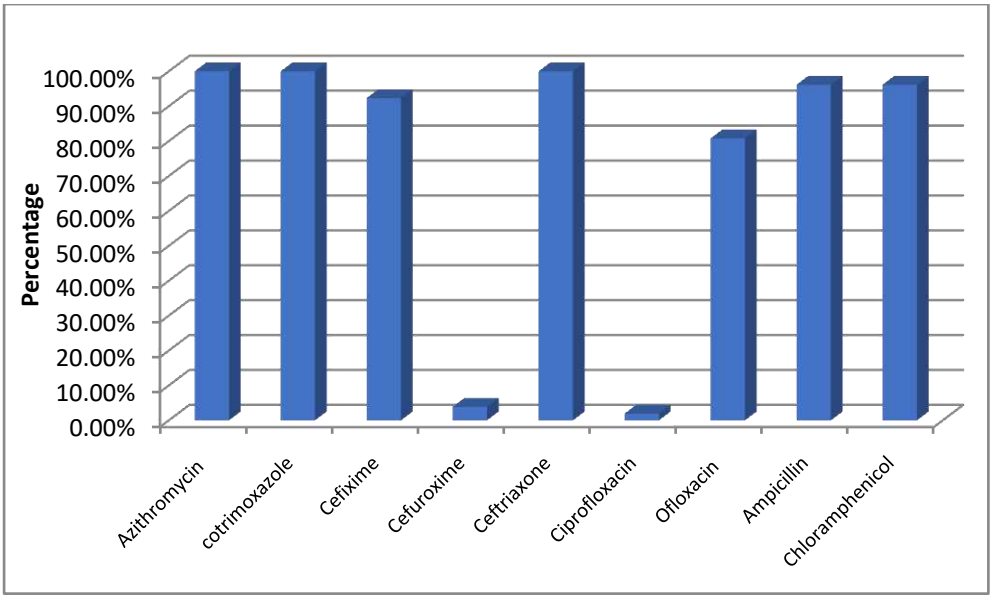



**Figure 22: Antibiotic Sensitivity Profile of Salmonella Typhi Isolates**

**Antibiotic sensitivity profile of Salmonella Paratyphi Isolates**

Of total 61 blood culture positive cases, 9 cases had blood culture positive for Salmonella Paratyphi

**Table 21: Antibiotic sensitivity profile of Salmonella Paratyphi isolates**

| | **salmonella parayphiA** | |
|---|---|---|
| | **Number of isolates** | **Percentage** |
| Azithromycin | 9 | 100.00% |
| cotrimoxazole | 9 | 100.00% |
| Cefixime | 9 | 100.00% |
| Cefuroxime | 0 | 0.00% |
| Ceftriaxone | 9 | 100.00% |
| Ciprofloxacin | 0 | 0.00% |
| Ofloxacin | 8 | 88.89% |
| Ampicillin | 6 | 66.67% |
| Chloramphenicol | 0 | 0.00% |
| Total | 9 | 100.00% |

**Azithromycin** came out to be sensitive in all 9 cultures of salmonella Paratyphi growth, being 100 % sensitive.

**Cotrimoxazole** has 100% sensitivity.

In **Cephalosporins** group, ceftriaxone and cefixime have maximum sensitivity of 100 percent with no sensitivity of cefuroxime.

**In Quinolone** group, Ofloxacin is sensitive in 88.8 % cases whereas Ciprofloxacin is resistant in all cases.

**Ampicillin** is sensitive in 66.6% cases.

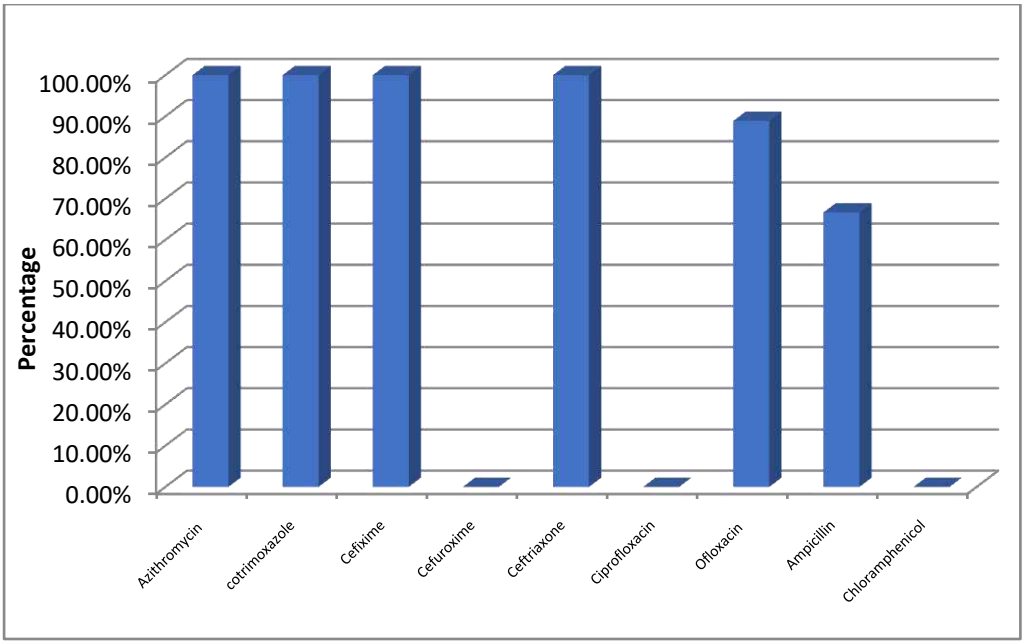



**Figure23: Antibiotic sensitivity profile of Salmonella Paratyphi Isolates**

**Table 22: Drug Resistance in Salmonella**

| | salmonella typhi | salmonella typhi | salmonella parayphiA | salmonella parayphiA |
|---|---|---|---|---|
| Ampicillin | 50 | 96.15% | 6 | 66.67% |
| cotrimoxazole | 52 | 100.00% | 9 | 100.00% |
| Azithromycin | 52 | 100.00% | 9 | 100.00% |
| Quinolones | 43 | 82.69% | 8 | 88.89% |
| Cephalosporins | | | | |
| Cefixime | 48 | 92.31% | 9 | 100.00% |
| Cefuroxime | 2 | 3.85% | 0 | 0.00% |
| Ceftriaxone | 52 | 100.00% | 9 | 100.00% |
| Chloramphenicol | 50 | 96.15% | 0 | 0.00% |

Comparison of Salmonella Typhi and Paratyphi sensitivity has been done and it has been observed that Amipicillin is more sensitive 96% in Typhi growth as compared to 66.6% sensitivity in Paratyphi cultures.

**Azithromycin** has same sensitivity 100 % in both typhoid and paratyphoid cultures.

**Cotrimoxazole** has 100% sensitivity in both Salmonella Typhi and Salmonella Paratyphi isolates.

**Quinolones** have better sensitivity in paratyphi isolates as compared to typhi isolates .88.8% paratyphoid cultures are sensitive against 82.6% sensitivity in typhoid cultures.

In **Cephalosporin group**, **Ceftriaxone** has same sensitivity of 100 % in both typhi and paratyphi isolates whereas **cefixime** has better sensitivity in paratyphoid isolates 100 % as compared to 92% in typhoid group.

**Cefuroxime** is resistant in all paratyphoid culture growths where as 3.8% typhoid cultures have still shown sensitivity.

Chloramphenicol has shown sensitivity in 96.1% Salmonella typhi cultures.

It is concluded that Salmonella Typhi is more resistant to Quinolones and cefixime as compared to Salmonella Paratyphi.

Salmonella Paratyphoid is more resistant to Ampicillin and Cefuroxime in comparison with Salmonella Typhi.

Both Salmonella Typhi and Paratyphi have not developed resistant against Azithromycin and Ceftriaxone.

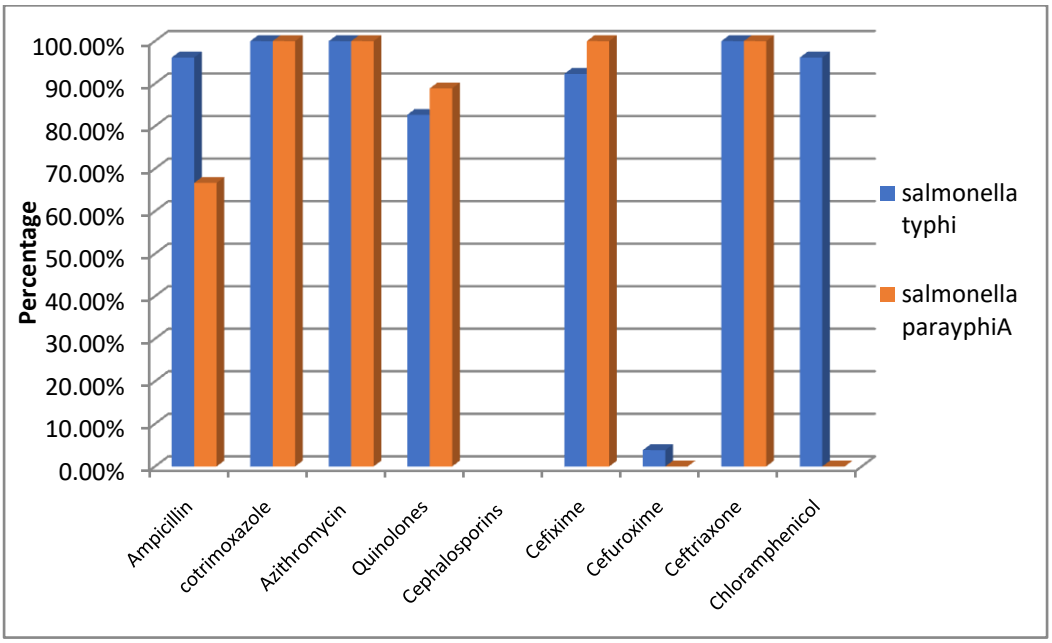



**Figure 24: Comparison of Drug Resistance in Salmonella Typhi and Salmonella Paratyphi isolates**

**Multi Drug Resistance**

Multi Drug Resistant Salmonella is defined as Salmonella isolates resistant to three group of antibiotics Chloramophenicol, Ampicillin and Cotrimoxazole.

In this study no isolate has resistance to all three antibiotics, henceforth MDR salmonella has not been detected in this study.

**Table 23: Comparison Of Widal and Blood Culture Positive cases**

| | no growth | salmonella parayphiA | salmonella typhi | Total |
|---|---|---|---|---|
| NEGATIVE | 0 | 0 | 6 | 6 |
| TO | 1 | 0 | 3 | 4 |
| TO+AH | 0 | 5 | 0 | 5 |
| TO+TH | 8 | 0 | 16 | 24 |
| NOT DONE | 0 | 4 | 27 | 31 |
| Total | 9 | 9 | 52 | 70 |

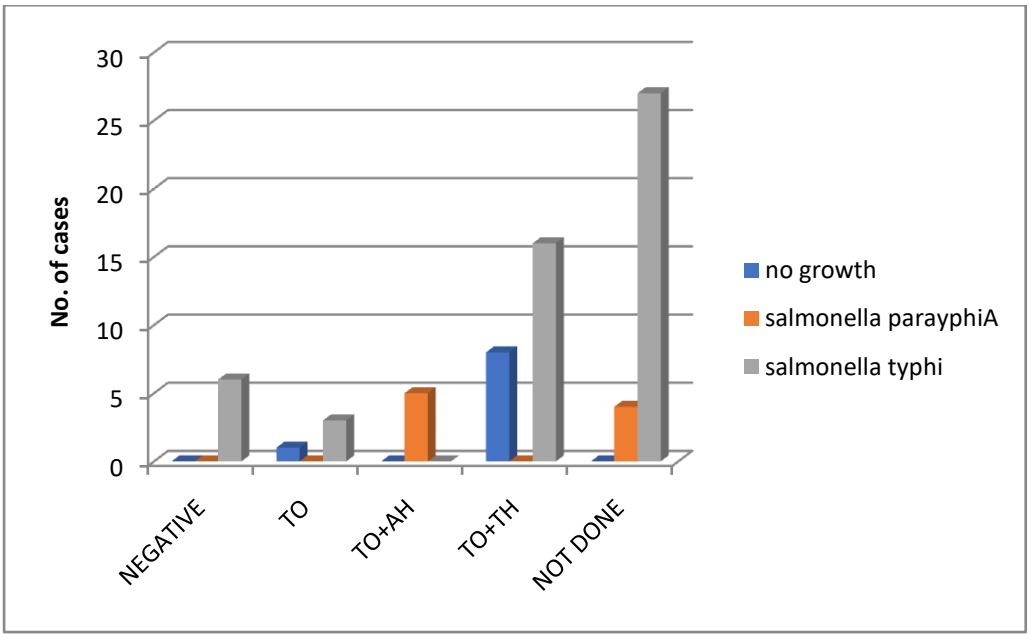



**Figure 25: Comparison Of Widal and Blood Culture Positive cases**

It is also compared that positive Widal test for typhoid fever cases had blood culture also positive for Salmonella typhi in 16 cases depicting that widal test must have taken in first week of illness. 8 cases with positive Widal test for typhoid fever had no growth.

Similarly it is compared for paratyphoid fever as well, of 5 cases with positive Widal test for paratyphoid fever, all cases had Salmonella paratyphi growth in their blood culture.

Of 4 cases with Widal titers positive for TO, 3 cases had growth of Salmonella typhi with 1 case of no growth.

In 6 cases where Widal titers came out to be negative , blood culture showed growth for Salmonella typhi , as these test must have been done in first week of illness when usually blood culture comes positive.

**Table 24: Usefulness of widal test in diagnosis of enteric fever**

| | Blood culture | | Total |
|---|---|---|---|
| **Widal** | **Positive** | **Negative** | |
| Positive | 24 | 9 | 33 |
| Negative | 6 | 0 | 6 |
| Total | 30 | 9 | 39 |

| Statistic | Value | 95% CI |
|---|---|---|
| Sensitivity | 80.00% | 61.43% to 92.29% |
| Specificity | 0.00% | 0.00% to 33.63% |
| Positive Likelihood Ratio | 0.8 | 0.67 to 0.96 |
| Negative Likelihood Ratio | | |
| Disease prevalence (*) | 76.92% | 60.67% to 88.87% |
| Positive Predictive Value (*) | 72.73% | 69.04% to 76.13% |
| Negative Predictive Value (*) | 0 | |
| Accuracy (*) | 61.54% | 44.62% to 76.64% |

Blood culture has been considered as gold standard test for Enteric fever for Typhoid and Paratyphoid fever diagnosis and if we compare serodiagnostic test, widal test with gold standard test then Widal test came out to be more sensitive test with zero specificity. Also it has more positive predictive value.

**Use Of Antibiotics**

Both i/v antibiotics and oral antibiotics are used during hospital stay.

Iv antibiotics, cephalosporins, have been given to the patients in our study.

i/v cefotaxim is given in 1 case making 1.4 % of total for 4 days.

I/v Cefepime tazobactum is being given in 4 cases, 2 cases were given antibiotic for 7 days and 2 cases were given antibiotics for 10 days.

i/v Ceftriaxone is sensitive in all blood culture growth and it is used in 62 cases .

In 1 case it is used in combination with oral azithromycin

And in 3 cases, both oral cefixime and i/v ceftriaxone is used.

**Table 25: Type of Antibiotics used.**

| Type Of antibiotic | No. of cases | Percentage |
|---|---|---|
| i/v Actamase | 4 | 5.7% |
| i/v ceftriaxone | 62 | 88.6% |
| i/v ceftriaxone , oral azithromycin | 1 | 1.4% |
| i/v ceftriaxone , oral cefixime | 3 | 4.3% |
| Total | 70 | 100.0% |

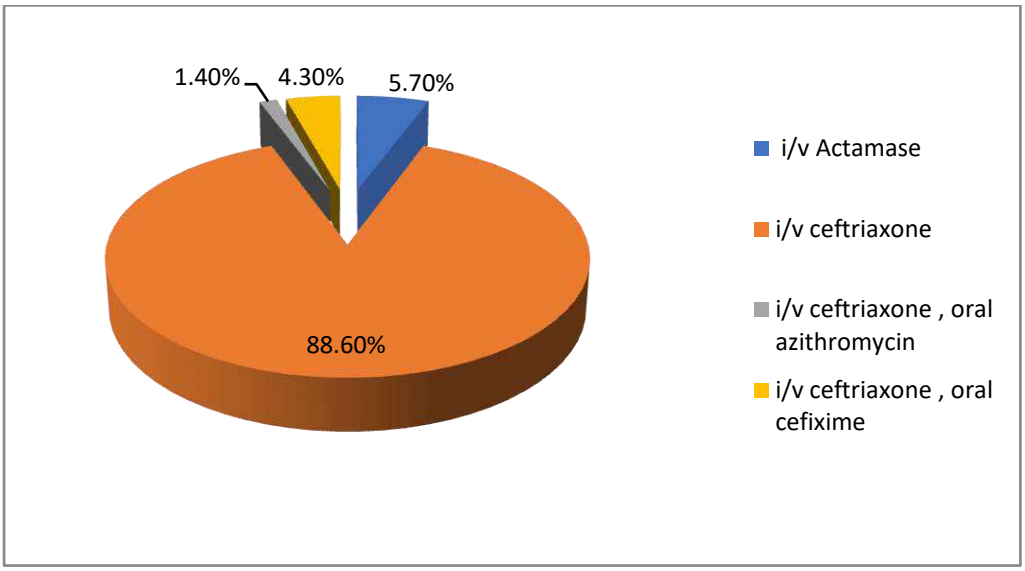



**Figure26: Type of Antibiotics used.**

**i/v Ceftriaxone Duration**

In Most cases , 37 cases were given i/v ceftriaxone for 7 days , 56.1 % of total followed by 8 cases , 12.1 % of total , where i/ ceftriaxone was given for 5 days .

In 5 cases, 7.6 % of total cases, iv ceftriaxone was given for 8 days followed by 9 and 10 days in 4 cases each making 6.1 % each.

**Table 26: Number of cases with use of I/V Ceftriaxone**

| Duration of Ceftriaxone | No. of cases | Percentage |
|---|---|---|
| 1 day | 1 | 1.5% |
| 3 days | 2 | 3.0% |
| 4 days | 3 | 4.5% |
| 5 adys | 8 | 12.1% |
| 7 days | 37 | 56.1% |
| 8 days | 5 | 7.6% |
| 9 days | 4 | 6.1% |
| 10 days | 4 | 6.1% |
| 13 days | 1 | 1.5% |
| Total | 66 | 100.0% |

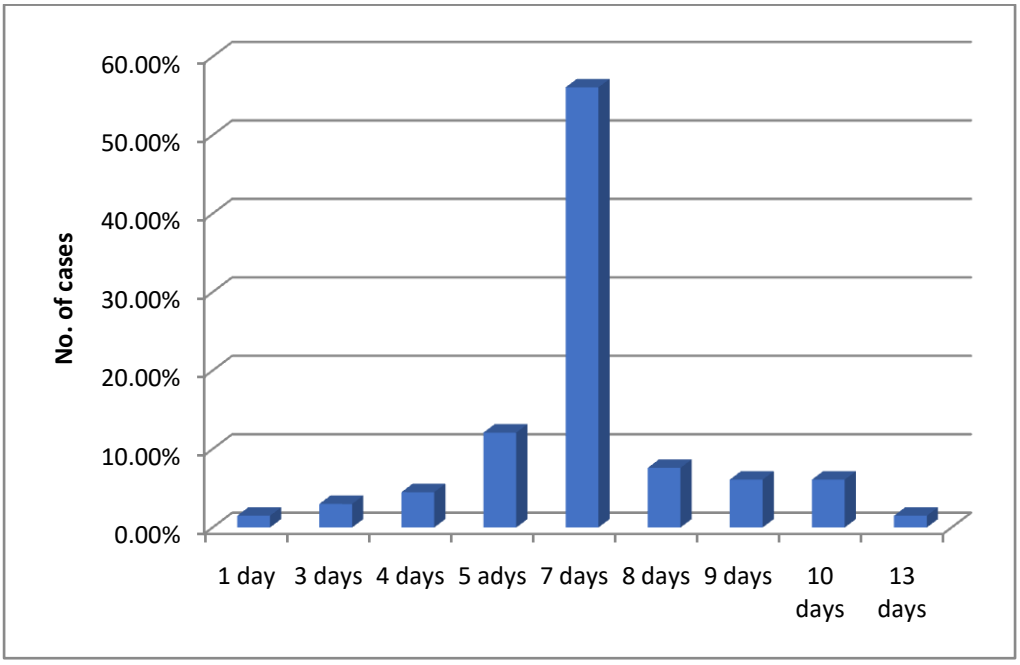



**Figure27: Number of cases with use of I/V Ceftriaxone**

Oral Aminoglycosides were given in 19 cases and all were given oral azithromycin and maximum cases 9, 12.9% of total received oral azithromycin for 5 days

**Day OfDefervescence of Fever**

Day of defervescence of fever has also impact on choice of antibiotic and duration of antibiotic use.

Maximum cases, 14 of total 70, making 20%, had defervescence of fever at day 12 followed by 9 cases, 12.9 % of total who had defervescence at day 11 of fever onset.

**Table 27: Duration of Day of Defervescence of Fever**

| Day of Defervescence of Fever | No. of cases | Percentage |
|---|---|---|
| | 1 | 1.4% |
| day 4 | 1 | 1.4% |
| day 5 | 2 | 2.9% |
| day 6 | 3 | 4.3% |
| day 7 | 3 | 4.3% |
| day 8 | 7 | 10.0% |
| day 9 | 4 | 5.7% |
| day 10 | 8 | 11.4% |
| day 11 | 9 | 12.9% |
| day 12 | 14 | 20.0% |
| day 13 | 8 | 11.4% |
| day 14 | 8 | 11.4% |
| day 15 | 2 | 2.9% |
| Total | 70 | 100.0% |

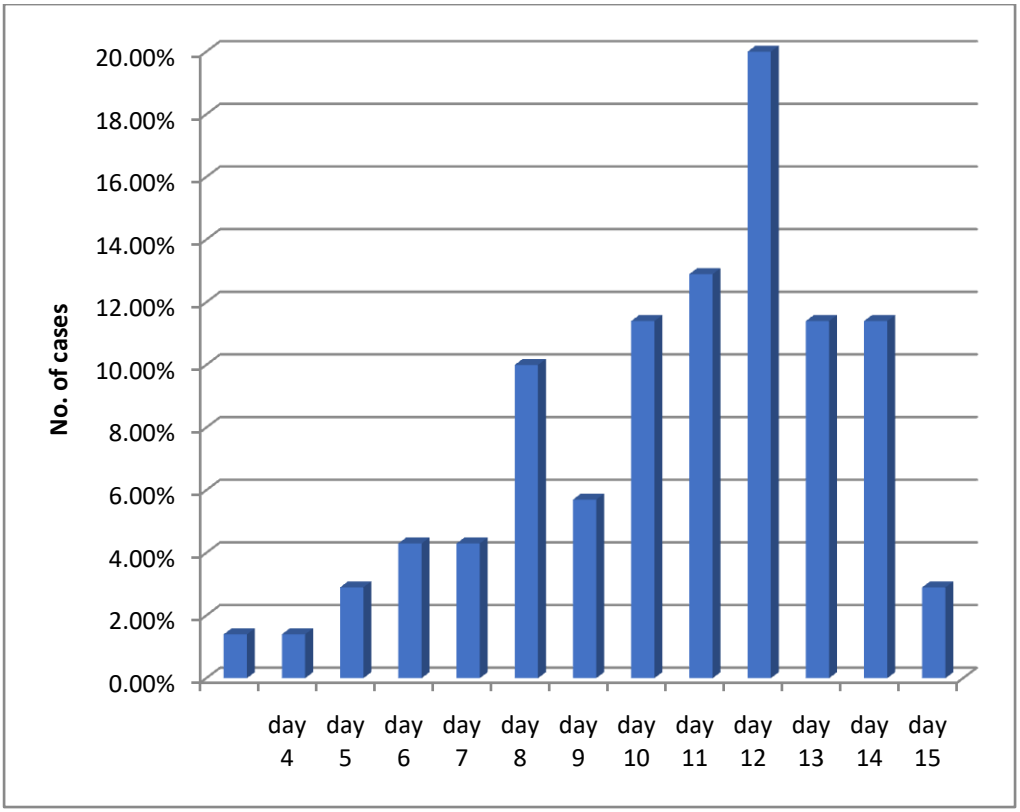



**Figure28: Duration of Day of Defervescence of Fever**

**Table 28: Significance of use of combination of Antibiotics**

| Antibiotics | Defervescence of Fever group | | Total | Chi-square value | p-value |
|---|---|---|---|---|---|
| | < 10 | > 10 | | | |
| Double | 7 | 14 | 21 | 0.81 | 0.667 |
| Single | 12 | 34 | 46 | | |
| Triple | 1 | 1 | 2 | | |
| Total | 20 | 49 | 69 | | |

Day of defervescence of fever was more than 10 days in 49 cases and less than 10 days in 20 cases.

It is not related with number of antibiotics used since, triple antibiotic use had same day of defervescence.In patients where one antibiotic is used 34 patients had defervescence after 10 days of fever and 12 patients had defervescence in less than 10 days.

In patients with two type of antibiotic use, defervescence of fever is more than 10 days in most cases, 14 of total 21 and 7 patients had defervescence of fever less than 10 days.

Henceforth duration is not shortened with use of combination of antibiotics.

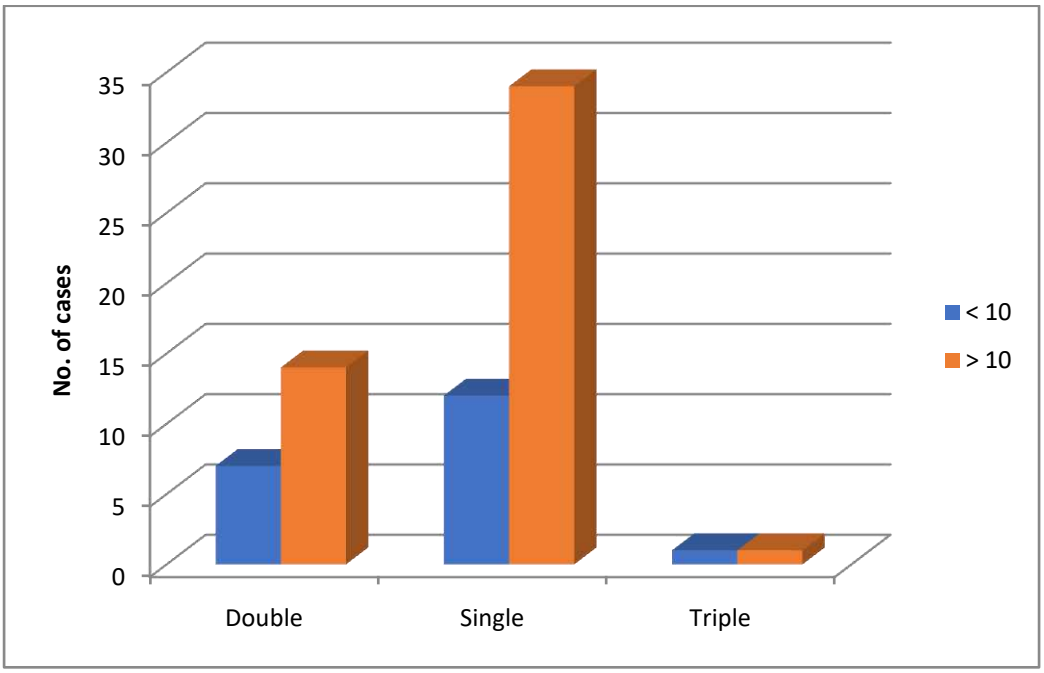



**Figure29: Significance of use of combination of Antibiotics**

**Table 29: Outcome of cases with Enteric Fever**

Out of total 70 patients admitted , 69 patients were discharged and 1 patient took discharge on request.

| Outcome | No. of cases | Percentage |
|---|---|---|
| Discharge | 69 | 98.6% |
| DOR | 1 | 1.4% |
| Total | 70 | 100.0% |

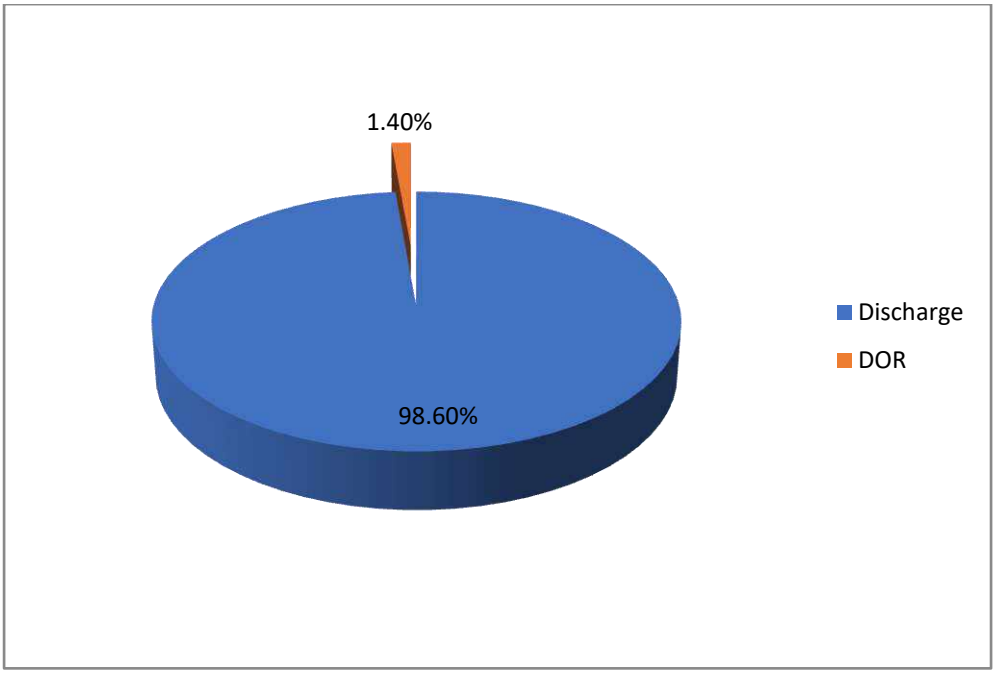



**Figure30: Outcome of cases with Enteric Fever**

# DISCUSSION

This descriptive study was conducted in the department of Paediatrics and Microbiology, Dayanand Medical College and Hospital, Ludhiana, Punjab, India. All confirmed and probable cases of Enteric fever admitted in the department of Paediatrics from month of February 2020 to month of August 2021 were included. This study was done to observe clinical profile of Enteric fever in children which is more common in resource-limited overcrowded communities with poor access to sanitation and management of which is compounded by the increasing antimicrobial resistance to the first-line antibiotics used. Keeping in view the global burden of enteric fever [59] and more prevelance in low socioeconomic countries, need for this study becomes more important.

In this study, total 70 cases were enrolled, 63 were confirmed cases with blood culture positive; 52 cases with blood culture positive for Salmonella typhi and 9 cases were blood culture positive for salmonella paratyphi and 9 cases were probable cases based on serodiagnosis Widal test and clinical profile.

Of total 70 admitted patients enrolled, 18 were in age group less than equal to 12 months of age, 25.7% of total cases, 19 were in age group 12 months to 60 months, accounting for 27.2% of total cases and maximum number of cases, 33 were in age group of more than 60 months, making 47.1% of total patients.

40 % of total, 28 cases were female patients and 60% of total, 42 cases were male patients.

All cases had fever at admission with a mean duration of 8 days .Fever was acute in onset in 62 cases (88.6%) patients and insidious in 8 patients (11.4 % of total).

Most cases 52.9%, had moderate grade of fever and 47.1% cases with high grade fever at admission, chills present in 15.7 % cases. Pain

abdomen was present in 22 cases accounting for 31.4 % of total. 50% patients had loose stools and vomitings associated. 21 cases with diarrhea had episodes lasting for 3 – 7 days and 14 cases had loose stools, vomitings episodes for less than 3 days.In all cases, vomitings were non bilious, non projectile, non blood stained. Out of total 70 cases, 5 had altered sensorium, 3 cases, 4.2 % of total with abnormal body movements, with 1 episode of uprolling of eyeballs. in Similar findings were seen in prospective observational study done by Ranganatha et al [60]in K Kempegowda Institute of Medical Sciences and Research Centre, Bangalore Karnataka, India where they enrolled 113 patients with Enteric fever and studied their clinical profile and found that all cases had fever at admission, with 44% patients with vomitings and 16 % with loose stools, 18% cases had pain abdomen and 61% cases with anorexia. There were no abnormal body movements in cases enrolled but headache was present in 12% cases. In contrary to my study their study had cough as presenting symptom in 10 % cases.

In this study, 20 cases had history of antibiotics intake prior to hospitalisation.18 cases (25.7%) had received oral antibiotics, 1 case (1.4%) had combined oral and iv antibiotic intake and 1 case (1.4%) with i/v antibiotic intake. Most of them had received antibiotic for 2 days prior to hospitalisation. 61 % cases had received oral cefixime followed by azithromycin in 16% cases, Ofloxacin in 1 case making 5.6% of total. i/v antibiotics used prior to hospitalisation in our hospital were ceftriaxone and vancomycin in 5.6% cases of total 20 cases with previous drug history.

Only 1 of the 70 patients was vaccinated against typhoid fever with typhoid conjugate vaccine before hospitalisation.

On examination, it was observed that no patient had icterus, 1.4% of total cases had edema. 47% cases had hepatomegaly and hepatosplenomegaly in 25.7 % cases. Similar results were also seen

in study done by Ranganatha et al [60] with hepatomegaly seen in 44% of cases, splenomegaly 21 % and hepatosplenomegaly in 16% cases.

Laboratory investigations showed that considerable number of cases had anemia with minimum hemoglobin being 5.1 gm% with mean value of 10.1gm%. leucocytosis has been noted with mean TLC of 10961. Eosinopenia was observed with minimum eosinophil count of 0.0, maximum being 14 and mean value of 0.43. Thrombocytopenia was seen in 17 cases. Similar results have been seen in prospective study done in Jakarta, Indonesia by Suhendro suwarto et al [61], where they investigated laboratory parameters to predict *Salmonella* bacteraemia. We conducted a prospective cohort study in Jakarta, Indonesia. Out of 187 individuals, 27 had *Salmonella typhi* and 12 had *S. paratyphi* in blood cultures and they noticed absolute eosinopenia, elevated aspartate aminotransferase and elevated C-reactive protein > 40 mg/L as positive predictors.

In our study, inflammatory markers, C – reactive protein was raised in 64 cases, 96.9% of total with maximum value of 234.3. LDH was also positive in 47 patients.

SGOT was elevated in 49 cases with mean value of 109.7 and SGPT was elevated in 40 with mean value of 89.6.

Serodiagnostic test Widal test was done in 39 patients. TO titers of more than 160 and TH titers of more than 160 were considered significant in our study in contrary to study done by Abraham et al [56] in Ethiopia where they considered titers more than equal to 160 as significant.

TO and TH titers depicted growth of Salmonella Typhi and came out to be positive in 61.5% of cases .TO and AH depicting Salmonella Paratyphi came out to be positive in 12.8 % of total cases and Widal test was negative in 15.3% cases. More false positives were found than false negatives in the study done in Ethiopia by Abraham et all

which was contrary to our study where we found more sensitivity, more true positives with more positive predictive value.

Another study to depict usefulness of Widal test in diagnosis of Enteric Fever was done by Susanta Kumar et al.[62] Their study was conducted at Tertiary Medical College Hospital, Dhaka to examine improvements in enteric fever clinical trends. Their research included a minimum of 120 children aged 0 to 14 with typhoid fever. For all, 90 children had definite diagnosis, as shown by S isolation for typhoid or paratyphoid fever and 30 were probable cases. The Widal research was performed using the quick diaphragm agglutination process and was tested in accordance with the results from blood cultivation. They observed that the accuracy of the widal tube and slide agglutination tests as used in the study in terms of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were 73%, 62%, 92% and 28%, respectively. In our study Widal came out to be more sensitive test with sensitivity of 80% and not a specific test as all widal negative cases had blood culture positive, being taken in first week of illness when we get blood culture positive results.

It was concluded that widal test, a large-scale test had importance as a typhoid fever diagnostics device, more flexible, cheaper and quicker than other molecular and serological studies.

Blood Culture was considered as Gold standard test for Enteric Fever. In our study, out of total 70 enrolled cases, 61 were culture positive, 52 cultures for Salmonella Typhi and 9 cases for Salmonella Paratyphi.

Sensitivity pattern was studied for both Salmonella Typhi and Paratyphi isolates, and it was seen that Cotrimoxazole, Azithromycin and ceftriaxone are 100 % sensitive for salmonella Typhi. Ampicillin and Chloramphenicol were sensitive in 96 % of isolates followed by cefixime which was sensitive in 92 % of cases. Ofloxacin was sensitive in 80% cases. Least sensitive drugs are cefuroxime followed by ciprofloxacin.

Sensitivity pattern study of salmonella paratyphi had shown 100% sensitivity of azithromycin, cotrimoxazole, cefixime and ceftriaxone followed by 88% sensitivity of ofloxacin and 66% of ampicillin.

We compared the resistance pattern of Salmonella Typhi and Salmonella Paratyphi isolates, Salmonella Typhi was more resistant to Quinolones and cefixime.

And Salmonella Paratyphi was more resistant to Ampicillin and Cefuroxime.Both Salmonella Typhi and Salmonella Paratyphi had no resistance against Azithromycin and Ceftriaxone.

In our study we compared i/v ceftriaxone and oral cefixime and found that ceftriaxone is 100% sensitive in both isolates whereas cefixime is 92%sensitive in Salmonella typhi isolate compred to 100 % sensitivity in Salmonella Paratyphi isolate but study conducted by Z A Bhutta[40,41] had different opinion. They randomly allocated 80 children with suspected multidrug-resistant tyhpoid fever to therapy with either cefixime or ceftriaxone. Of these, an alternative diagnosis was subsequently made in 10 children and another 10 were excluded because cultures were negative. In 9 cases the typhoidal organisms isolated were susceptible to first-line drugs. In all, 50 children were randomly allocated to receive therapy with either intravenous ceftriaxone (65 mg/kg/day once daily, Group A, n = 25) or oral cefixime (10 mg/kg/day divided every 12 hours, Group B, n = 25) for 14 days. The two groups were comparable in their clinical characteristics, duration and severity of illness at the time of admission. The time to defervescence was comparable in both groups (8.3 +/- 3.7 vs. 8.0 +/- 4.1 days, P = not significant). An equal number (3 in each group) failed to respond and underwent a change in therapy. Three children in Group A and one in Group B relapsed. They concluded that oral cefixime can be used as effectively as parenterally administered ceftriaxone for management of typhoid fever in children.

In our study no isolate had Multi Drug Resistance, as not even a single isolate was resistant to all three antibiotics Chloramphenicol, Ampicillin and Cotrimoxazole which define multi drug resistance whereas study conducted by Jared McAteer et al[41]for multi drug resistant salmonella isolates and their relation with travellers and unvaccinated children depicted that out of 2003 isolates tested for antimicrobial susceptibility, 1216 (61%) were fluoroquinolone-nonsusceptible, of which 272 (22%) were also resistant to ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole (multidrug-resistant [MDR]). All were susceptible to ceftriaxone and azithromycin. MDR and fluoroquinolone-nonsusceptible isolates were more common in children than adults (16% vs 9%, P < .001, and 61% vs 54%, P < .001, respectively). Fluoroquinolone nonsusceptibility was more common among travel-associated than domestically acquired cases (70% vs 17%, P < .001). They concluded that approximately 95% of currently vaccine-eligible pediatric travelers were unvaccinated, and antimicrobial-resistant infections were common so New public health strategies are needed to improve coverage with currently licensed vaccines. Introduction of an effective pretravel typhoid vaccine for children <2 years could reduce disease burden and prevent drug-resistant infections.

Observing this sensitivity profile, i/v ceftriaxone was used in 88.6% of our cases and maximum number of cases had received i/v ceftriaxone for 7 days. Contrary to our study, Robert W Frenck [35]did randomised controlled study for difference between ceftriaxone and azithromycin for uncomplicated typhoid fever. During the study period, all children of 4–17 years of age who had a clinical diagnosis of typhoid fever were included. Eligibility for enrollment required that a subject have a documented fever (temperature, ⩾38.5°C) and a history of fever for at least 4 days plus at least 2 of the following criteria: abdominal tenderness, hepatomegaly, splenomegaly, and/or rose spots.

They concluded that azithromycin given for 7 days at a dosage of 10 mg/kg/day (maximum dose, 500 mg/day) appears to be highly effective

for the treatment of uncomplicated typhoid fever in children, with clinical cure rates comparable to those for ceftriaxone. Once-daily administration of oral azithromycin had simple treatment regimen for typhoid fever caused by either susceptible or drug-resistant strains of *S. typhi* and was suitable for use in areas where medical resources are limited.

But supporting our study, use of antibiotics by Dutta et al [36]in their study was similar. The isolated strains of S. typhi were tested for in vitro antimicrobial susceptibility in their study. They observed that clinical and bacteriological cure was observed with intravenous ceftriaxone therapy in all the 32 bacteriologically positive patients so i/v ceftriaxone was used even in MDR salmonella strains.

Combination antibiotics were also used, i.v ceftriaxone and oral azithromycin but duration of defervescence of fever was not shortened with combination antibiotics. Maximum cases had day of defervescenceat day 12 of onset of fever.

We discharged 98.6% cases and 1.4% cases went discharge on request. No mortality was encountered in this study.

# SUMMARY AND CONCLUSION

In conclusion, Enteric fever is a community acquired systemic infection, common in developing countries with rising antimicrobial resistance. In our study Enteric fever was more common in male than female children. Children of age group more than 60 months were more affected. With Fever at presentation, acute in onset in 88% cases, moderate in grade in 52.9% cases, associated with pain abdomen in 31.4% cases and loose stools and vomitings in 50% cases. Encephalopathy was observed in only 4.2% cases. 28% cases had history of antibiotic intake prior to hospitalization. 70% of them had received cefixime.Only one case had received conjugate typhoid vaccine. On examination, anemia was a common sign, mild in 57.4% cases, 1.4% cases had edema. Hepatomegaly was more common feature than hepatosplenomegaly. In laboratory investigations, mean hemoglobin seen was 10.1, Eosinopenia was observed with minimum eosinophil count of 0.0 inflammatory markers, C – reactive protein was raised in 64 cases, 96.9% of total with maximum value of 234.3. LDH was also positive in 47 patients.

SGOT was elevated in 49 cases with mean value of 109.7 and SGPT was elevated in 40 with mean value of 89.6. Serodiagnosis was done in 39 cases using Widal test which had 80% sensitivity and 74.3% positive predictive value. Blood culture for Salmonella isolates was considered gold standard test and was positive in 87.2 % of total cases. Antibiotic sensitivity profile was studied for both Typhi and Paratyphi isolates. Azithromycin, Ceftriaxone and cotrimoxazole had 100% sensitivity. In comparison between Salmonella typhi and salmonella Paratyphi, Typhi isolates were more resistant to Quinolones and Cefixime and Paratyphi isolates were more resistant to Ampicillin and Cefuroxime.No isolate was Multi drug resistant. Using this sensitivity profile, i/v ceftriaxone was used in 88.6% cases. Combination antibiotic had no impact on decreasing duration of day of defervescence of fever . All patients were discharged. Further studies

are required on larger cohorts for antibiotic sensitivity profile of Multi Drug Resistant Salmonella and Extensively Drug Resistant Salmonella.

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# PROFORMA

Name: MRD No.

| Age | Sex |
|---|---|
| DOA | DOD |

Residence:

Month:

Hospital stay:

| Anthropometry. | Actual | Expected. | Remarks |
|---|---|---|---|
| Weight (Kg) | | | |
| Height/Length(cm) | | | |
| Head Circumference (cm) | | | |
| BMI | | | |

**Fever**

1. Duration
2. Onset
3. Grade
4. Type
5. Rigors /Chills

**Signature of candidate :** **Signature of consultant:**

6. Pain Abdomen
7. Loose stools /Vomitings
8. Unconsciousness /Seizures

**Past Drug History**

**Type of Antibiotic taken**

**Duration of Antibiotic**

**Vaccination History**

**GPE**

- Anaemia /Icterus/Edema: Face /Feet
- Vitals : HR : BP : Temp .
- CFT
- Chest:
- CVS :
- P/A : Liver /Spleen /Ascites
- CNS :AVPU / GCS

**INVESTIGATIONS**

| | |
|---|---|
| **Hb/MCV :**<br>**Anaemia** | **Septic markers**<br>**CRPq**<br>**ESR** |
| **TLC**<br>**N/L/M/E** | **LFTs**<br>**TSB/DSB:** |

**Signature of candidate :**

**Signature of consultant:**

| | |
|---|---|
| | ALP |
| Platelets | Widal Titers<br>TO /TH/AH/BH |

**Blood culture and sensitivity**

| |
|---|
| |

**Treatment**

**Antibiotics Used**

**Type of Antibiotic** **Duration of antibiotic used**

Cefotaxime

Ceftriaxone

Ofloxacin

Ciprofloxacin

Aminoglycosides

**Days of Defervescence:**

**Outcome**

**DOR/LAMA**

- FINAL DIAGNOSIS

Signature of candidate :

Signature of consultant:

| Sr. No | MRD | Age (months ) | Sex | DOA | DOD | Hospital stay ( days ) | Actual Weight (Kg) | Actual Height/ Length(cm) | Actual Head Circumference (cm) | Actual BMI | Expected Weight (Kg) | Expected Height/ Length(cm) | Expected Head Circumference (cm) | Expected BMI | Fever Duration ( days ) | Onset | Grade | Type | Rigors/Chill | Pain Abdomen | Characteristics of Pain Abdomen |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 893068 | 60 | male | 05-02-2020 | 15-02-2020 | 11 | 19.7 | 114 | 50 | 18.6 | 17 | 108 | 50 | 14.7 | 5 | acute | moderate | intermittent | not present | present | mild , in epigastrium , no aggravating, relieving factors |
| 2 | 199481 | 48 | male | 06-02-2020 | 10-02-2020 | 5 | 13 | 103 | 50 | 12.26 | 16.1 | 102.7 | 49 | 15.4 | 6 | acute | moderate | intermittent | not present | not present | - |
| 3 | 67792 | 84 | male | 07-02-2020 | 13-02-2020 | 7 | 26 | 132 | 50 | 14.9 | 31.1 | 137 | 50 | 16.9 | 10 | acute | moderate | intermittent | not present | not present | - |
| 4 | 828614 | 12 | female | 17-02-2020 | 26-02-2020 | 10 | 10 | 79 | 47 | 16.1 | 9.8 | 78.6 | 45.9 | 16.3 | 5 | acute | moderate | intermittent | not present | not present | - |
| 5 | 919443 | 15 | female | 20-03-2020 | 30-03-2020 | 11 | 9 | 75 | 46 | 16.07 | 9.4 | 76 | 45.4 | 16.4 | 1 | acute | high | intermittent | not present | not present | - |
| 6 | 920385 | 36 | male | 26-03-2020 | 30-03-2020 | 5 | 12 | 91 | 48 | 14.6 | 15.8 | 101.6 | 50 | 15.4 | 10 | acute | high | intermittent | not present | not present | - |
| 7 | 920163 | 180 | male | 23-03-2020 | 31-03-2020 | 9 | 49.8 | 168 | 50 | 17.6 | 53.1 | 164 | 50 | 19.3 | 6 | acute | high | intermittent | not present | not present | - |
| 8 | 921515 | 108 | female | 07-04-2020 | 14-04-2020 | 8 | 8.5 | 68 | 47 | 18.4 | 8 | 70 | 45 | 16.3 | 7 | acute | moderate | intermittent | not present | present | mild , in epigastrium , non radiating , no aggravating , releiving factors |
| 9 | 922250 | 60 | male | 14-04-2020 | 23-04-2020 | 10 | 17 | 106 | 50 | 15.1 | 17.1 | 110 | 50.7 | 14.1 | 7 | acute | moderate | intermittent | present | present | mild , since 2 days , in epigastrium , non radiating , no aggravating , releiving factors |
| 10 | 86946 | 72 | male | 16-04-2020 | 23-04-2020 | 8 | 16.3 | 111 | 50 | 13.2 | 20.7 | 117.8 | - | 15 | 5 | acute | moderate | intermittent | not present | present | mild , in epigastrium , non radiating , no aggravating , releiving factors |
| 11 | 920006 | 132 | female | 23-03-2020 | 29-03-2020 | 7 | 40 | 142 | - | 19.9 | 35.4 | 143.5 | 50 | 17.1 | 2 | acute | high | intermittent | not present | present | mild , since last 4 days, in epigastrium , non radiating , no aggravating , releiving factors |
| 12 | 938755 | 96 | male | 29-06-2020 | 15-07-2020 | 17 | 18 | 118 | - | 13.8 | 24 | 125 | - | 14 | 7 | acute | moderate | intermittent | not present | present | mild , in epigastrium , since last 3 days , non radiating , no aggravating , releiving factors |
| 13 | 930864 | 47 | male | 01-06-2020 | 13-06-2020 | 13 | 11 | 89 | 47.5 | - | 16.5 | 104 | 50 | - | 5 | acute | high | intermittent | not present | present | mild , in epigastrium , no aggravating, relieving factors |
| 14 | 312967 | 45 | male | 20-10-2020 | 24-10-2020 | 5 | 17.1 | 106 | 50 | - | 16 | 102 | 50 | - | 6 | acute | moderate | intermittent | not present | present | mild , in epigastrium , no aggravating, relieving factors |
| 15 | 992720 | 24 | male | 27-11-2020 | 27-11-2020 | 12 | 8.5 | 77 | 45 | - | 12.2 | 87.8 | 48 | - | 45 | insidious | moderate | intermittent | not present | not present | - |

| Sr. No | MRD | Loose Stools / Vomitings | Loose stools /Vomitings EPISODES | Unconsciousness /Seizures | Past Drug History | Type of Antibiotic taken | Duration of Antibiotic | Vaccination History | Anaemia | Icterus | Edema: Face /Feet | HR | SBP | DBP | Temp | CFT | Chest | CVS | Liver /Spleen /Ascites | AVPU / GCS | Hb | MCV |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 893068 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 112 | 100 | 60 | 98.4 | 2 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 9.2 | 67.2 |
| 2 | 199481 | not present | - | not present | oral antibiotics | azithromycin | 5 | Not vaccinated for typhoid | pallor + | not present | not present | 118 | 100 | 60 | 97 | 2 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver palpable 4 cm below RCM | 15 | 11 | 76.1 |
| 3 | 67792 | present | vomitin .gs x 3 days , non bilious , non projectile , 4 - 5 episodes /day , non blood stained | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 110 | 100 | 60 | 98.4 | 2 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver palpable 2 cm below RCM | 15 | 9.9 | 72.4 |
| 4 | 828614 | present | vomitings x 4 days , non bilious , non projectile , 3 - 4 episodes / day ; Loose stools x 2 days , watery , yellowish , non blood stained , 4 - 5 episodes / day . | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 146 | 90 | 60 | 98.4 | 2 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 8 | 25.7 |
| 5 | 919443 | not present | - | rmal body movements , up | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 188 | 90 | 60 | 103.6 | 2 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | liver 3 cm palpable below RCM , spleen non palpable | 15 | 8.5 | 71.4 |
| 6 | 920385 | present | Vomitings x 6 days , non bilious , non projectile , 3 - 4 episodes/ day , | rmal body movements , up | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 160 | 90 | 60 | 96 | 2 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 14 | 10.3 | 81.6 |
| 7 | 920163 | present | vomitings x 2 days , non projectile , non bilious | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | - | not present | not present | 124 | 100 | 70 | 103 .6 | 2 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 13 | 85.7 |
| 8 | 921515 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 140 | 80 | 50 | 99 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 2 cm below RCM , spleen non palpable | 15 | 8.7 | 67.6 |
| 9 | 922250 | not present | - | not present | oral antibiotics | Azee | 5 | Not vaccinated for typhoid | pallor + | not present | not present | 116 | 90 | 60 | 97 . 4 | 2 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 5 cm below RCM , spleen tip palpable | 15 | 7.1 | 78.7 |
| 10 | 86946 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 138 | 100 | 60 | 101 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 10.5 | 71.5 |
| 11 | 920006 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 88 | 110 | 70 | 100.2 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver plapable 4 cm below RCM , spleen non palpable | 15 | 8.7 | 86 |
| 12 | 938755 | present | 4 - 5 episodes / day , watery in consistency , non blood stained . | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 98 | 100 | 60 | 100 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 7.5 | 186 |
| 13 | 930864 | not present | - | not present | oral antibiotics | Ofloxacin | 5 | Not vaccinated for typhoid | pallor + | not present | not present | 142 | 100 | 60 | 102.2 | 3 | b/l air entry + ,reduced at lung bases , b/l conducted sounds + | S1 , S2 normal , no murmur | Liver 4 cm below RCM , spleen tip palpable | 15 | 7.5 | 64.9 |
| 14 | 312967 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 124 | 100 | 60 | 98.2 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 11.2 | 35.1 |
| 15 | 992720 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 130 | 100 | 60 | 100 | 3 | b/l air entry + , reduced on left side , No added sounds | S1 , S2 normal , no murmur | liver 3 cm palpable below RCM , spleen non palpable | 15 | 11.8 | 78.8 |

| Sr. No | MRD | Anemia | TLC | N | L | M | E | Platelets | CRPq | ESR | LDH | SGOT | SGPT | ALP | TO | TH | AH | BH | Blood Culture | Azithromycin | cotrimoxazole | Ceftriaxone | Ciprofloxacin | Ofloxacin | Ampicillin | Cefixime | Cefuroxime | Chloramphenicol | Cefotaxime |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 893068 | moderate | 6600 | 70.9 | 22.9 | 5.8 | 0.1 | 364000 | - | - | 348 | 59 | 48 | - | 40 | 160 | <20 | nil | salmonella typhi | S | S | S | R | S | S | S | R | R | - |
| 2 | 199481 | Mild | 7100 | 49.9 | 42.1 | 7.7 | 0.1 | 357000 | 12.52 | - | 520 | 69 | 68 | - | 40 | 160 | <20 | nil | no growth | - | - | - | - | - | - | - | - | - | - |
| 3 | 67792 | moderate | 5100 | 62.4 | 27.1 | 10.2 | 0 | 213000 | - | - | - | - | - | - | - | - | - | - | salmonella typhi | S | S | S | S | S | S | S | S | S | - |
| 4 | 828614 | moderate | 5100 | 52.1 | 41.7 | 5.8 | 0 | 225000 | 93.6 | - | 444 | 62 | 49 | - | 640 ET | 320 ET | <20 | nil | salmonella typhi | S | S | S | S | S | S | S | S | S | - |
| 5 | 919443 | moderate | 17600 | 32.9 | 56.7 | 9.2 | 1.1 | 277000 | 3.77 | - | - | 275 | 843 | 277 | ND | ND | ND | ND | salmonella typhi | S | S | S | R | S | S | S | R | S | i/v cefotaxim |
| 6 | 920385 | Mild | 3990 | 31.7 | 58.6 | 6.8 | 0.5 | 90,000 | 108 | - | 1355 | 193 | 82 | - | 160 | 320 ET | <20 | nil | salmonella typhi | S | S | S | R | S | S | S | S | S | - |
| 7 | 920163 | Mild | 7300 | 83.5 | 11 | 5.3 | 0 | 212000 | 93.6 | - | 319 | 42 | 42 | - | 320 ET | 80 | <20 | nil | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 8 | 921515 | moderate | 20100 | 54.3 | 37 | 8.6 | 0 | 2900000 | 35.2 | 2 | 582 | 171 | 245 | 212 | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 9 | 922250 | moderate | 5800 | 53.2 | 42.1 | 4 | 0.3 | 110000 | 103 | - | 563 | - | - | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 10 | 86946 | Mild | 13500 | 40.5 | 48.6 | 10.3 | 0.2 | 461000 | 150 | - | - | - | - | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 11 | 920006 | moderate | 7600 | 59.5 | 37.5 | 2.6 | 0.1 | 18000 | 134 | - | - | 368 | 86 | 274 | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 12 | 938755 | moderate | 7600 | 50.5 | 41.2 | 7.1 | 1.1 | 116000 | 41.08 | - | - | - | - | - | 256 0 ET | 2560 ET | 2560ET | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 13 | 930864 | moderate | 5200 | 72.7 | 12 | 14.5 | 0.2 | 60,000 | 163 | - | - | - | - | - | 640 ET | 1260 ET | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 14 | 312967 | Mild | 7500 | 65.3 | 28.6 | 5.7 | 0 | 186000 | 30.7 | - | 401 | 67 | 50 | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 15 | 992720 | Mild | 6500 | 43.7 | 42.9 | 13 | 0.1 | 339000 | 59.7 | - | - | - | - | 105 | - | - | - | - | salmonella parayphiA | S | S | S | R | S | R | S | R | S | - |

| Sr. No | MRD | Duration | Cefepime tazobactum | Duration | Ceftriaxone | Duration | Ofloxacin | Duration | Ciprofloxacin | Duration | Aminoglycosides | Duration Of antibiotics Intake | Antibiotics | No of Antibiotics | Days of Deffervesence of Fever | Deffervesence of Fever group | Outcome | FINAL DIAGNOSIS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 893068 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | oral azithromycin | 4 days | Inj Ceftriaxone,oral azithromycin | Double | 12 | 2 | Discharge | Typhoid Fever with Iron deficiency anemia |
| 2 | 199481 | - | - | - | Inj Ceftriaxone | 5 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 10 | 2 | Discharge | Typhoid Fever |
| 3 | 67792 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 12 | 2 | Discharge | Typhoid Fever |
| 4 | 828614 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 14 | 2 | Discharge | Typhoid Fever with Iron deficiency anemia |
| 5 | 919443 | 4 days | i/v actamase | 7 days | - | - | - | - | - | - | oral azithromycin | 2 days | i/v cefotaxim,i/v actamase,oral azithromycin | Triple | 6 | 1 | Discharge | Complicated Typhoid Fever with Typical Febrile Convulsions with Iron deficiency anemia |
| 6 | 920385 | - | - | - | Inj Ceftriaxone | 4 days | - | - | - | - | oral azithromycin | 4 days | Inj Ceftriaxone,oral azithromycin | Double | 7 | 1 | Discharge | Complicated Typhoid Fever with Enteric Encephalopathy |
| 7 | 920163 | - | - | - | Inj Ceftriaxone | 5 days | - | - | - | - | oral azithromycin | 7 days | Inj Ceftriaxone,oral azithromycin | Double | 6 | 1 | Discharge | Typhoid Fever |
| 8 | 921515 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 12 | 2 | Discharge | Typhoid Fever |
| 9 | 922250 | - | i/v actamase | 10 days | - | - | - | - | - | - | oral azithromycin | 7 days | i/v actamase,oral azithromycin | Double | 14 | 2 | Diischarge | Complicated Typhoid Fever with Pleural Effusion with Ascites with Respiratory Distress |
| 10 | 86946 | - | i/v actamase | 7 days | - | - | - | - | - | - | - | - | i/v actamase | Single | 12 | 2 | Discharge | Typhoid Fever |
| 11 | 920006 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | oral azithromycin | 5 days | Inj Ceftriaxone,oral azithromycin | Double | 8 | 1 | Discharge | Complicated Typhoid Fever with Thrombocytopenia |
| 12 | 938755 | - | i/v actamase | 8 days | Inj Ceftriaxone | 9 adys | - | - | - | - | oral azithromycin | 7 days | i/v actamase,Inj Ceftriaxone,oral azithromycin | Triple | 14 | 2 | Diischarge | Complicated Typhoid Fever with Leptospirosis with Hepatitis A with Anemia |
| 13 | 930864 | - | - | - | Inj Ceftriaxone | 13 days | - | - | - | - | oral azithromycin | 13 days | Inj Ceftriaxone,oral azithromycin | Double | 13 | 2 | Discharge | Complicated Typhoid Fever with Respiratory Distress with Thrombocytopenia with severe anemia with Grade 2 PEM with Hypovitaminosis D |
| 14 | 312967 | - | - | - | Inj Ceftriaxone | 4 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 8 | 1 | Discharge | Typhoid Fever |
| 15 | 992720 | - | - | - | Inj Ceftriaxone | 10 days , syp cefixime x 4 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 14 | 2 | Diischarge | Paratyphoid Fever with Neuroblastoma |

| Sr. No | MRD | Age (months ) | Sex | DOA | DOD | Hospital stay ( days ) | Actual Weight (Kg) | Actual Height/ Length(cm) | Actual Head Circumference (cm) | Actual BMI | Expected Weight (Kg) | Expected Height/ Length(cm) | Expected Head Circumference (cm) | Expected BMI | Fever Duration ( days ) | Onset | Grade | Type | Rigors/Chill | Pain Abdomen | Characteristics of Pain Abdomen |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 16 | 9911963 | 168 | female | 02-12-2020 | 09-12-2021 | 8 | 48 | 150 | - | 21.3 | - | - | - | - | 60 | insidious | moderate | intermittent | not present | present | mild , in epigastrium , no aggravating, relieving factors |
| 17 | 996230 | 35 | male | 06-12-2020 | 10-12-2020 | 5 | 14.2 | 99 | 47 | - | 14 | 95 | 49 | - | 12 | acute | high | intermittent | not present | not present | - |
| 18 | 748178 | 101 | male | 09-12-2020 | 13-12-2021 | 5 | 21 | 115 | - | 15.9 | 27 | 131.6 | - | 15.4 | 7 | acute | high | intermittent | not present | present | mild , in epigastrium , no aggravating, relieving factors |
| 19 | 997791 | 24 | male | 10-12-2020 | 17-12-2020 | 8 | 13.5 | 88 | 49 | 17.5 | 12 | 86.9 | 48.1 | - | 7 | acute | moderate | intermittent | not present | present | mild , in epigastrium , no aggravating, relieving factors |
| 20 | 1004088 | 180 | male | 23-12-2020 | 30-12-2021 | 8 | 55 | 176 | - | 17.7 | 56 | 166 | - | - | 15 | acute | high | intermittent | present | not present | - |
| 21 | 1005164 | 120 | male | 26-12-2020 | 28-12-2020 | 3 | 32 | 145 | - | 15.23 | 31 | 137 | - | 16.4 | 6 | acute | high | intermittent | not present | not present | - |
| 22 | 1006828 | 59 | male | 30-12-2020 | 07-01-2021 | 9 | 20 | 52 | - | 17.2 | 17.1 | 108 | - | 14.7 | 3 | acute | moderate | intermittent | not present | not present | - |
| 23 | 1007436 | 144 | male | 01-01-2020 | 08-01-2021 | 8 | 40 | 153 | - | 17.08 | 39 | 148 | - | 17.6 | 15 | acute | moderate | intermittent | not present | not present | - |
| 24 | 3624 | 120 | female | 03-01-2021 | 11-01-2021 | 9 | 25 | 141 | - | 12.62 | 33.2 | 140.4 | - | 16.8 | 60 | insidious | moderate | intermittent | not present | not present | - |
| 25 | 1009264 | 144 | male | 06-01-2021 | 13-01-2021 | 8 | 38 | 142.5 | - | 18.9 | 41 | 152 | - | 17.9 | 4 | acute | high | intermittent | not present | not present | - |
| 26 | 1009172 | 108 | female | 06-01-2021 | 16-01-2021 | 11 | 22 | 130 | - | 13.7 | 29 | 134 | - | 16.1 | 3 | acute | moderate | intermittent | present | not present | - |
| 27 | 1011789 | 156 | male | 12-01-2021 | 19-01-2021 | 8 | 53 | 169 | - | 18.5 | 54 | 157 .2 | - | 18.5 | 18 | insidious | moderate | intermittent | not present | not present | - |
| 28 | 1011696 | 17 | male | 16-01-2021 | 25-01-2021 | 10 | 9.5 | 80 | 45 | - | 10 | 80 | 46.5 | - | 12 | insidious | moderate | intermittent | not present | not present | - |
| 29 | 1020943 | 132 | female | 01-02-2021 | 01-02-2021 | 1 | 35 | 140 | - | 17.8 | 36 | 142 | - | 15.4 | 7 | insidious | high | intermittent | not present | not present | - |
| 30 | 1021465 | 48 | male | 02-02-2021 | 10-02-2021 | 9 | 13 | 85 | - | - | 14.6 | 97 | 49 | - | 10 | acute | moderate | intermittent | not present | not present | - |
| 31 | 999472 | 19 | male | 05-02-2021 | 11-02-2021 | 7 | 12 | 91 | 46 | - | 10.5 | 82 | 46.5 | - | 6 | acute | high | intermittent | present | not present | - |
| 32 | 1025398 | 22 | male | 09-02-2021 | 16-02-2021 | 8 | 10 | 85 | 50.5 | 13.8 | 11.5 | 86 | 48 | 15.75 | 10 | acute | moderate | intermittent | not present | not present | - |
| 33 | 127767 | 69 | female | 12-02-2021 | 18-02-2021 | 7 | 14 | 109 | 48 | 11.86 | 17.6 | 110 | 50 | 14.54 | 7 | acute | high | intermittent | not present | not present | - |

| Sr. No | MRD | Loose Stools / Vomitings | Loose stools /Vomitings EPISODES | Unconsciousness /Seizures | Past Drug History | Type of Antibiotic taken | Duration of Antibiotic | Vaccination History | Anaemia | Icterus | Edema: Face /Feet | HR | SBP | DBP | Temp | CFT | Chest | CVS | Liver /Spleen /Ascites | AVPU / GCS | Hb | MCV |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 16 | 9911963 | present | vomitings present , 3 episodes per day , non bilious , non projectile , non blood stained | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | - | not present | not present | 80 | 120 | 80 | 98.2 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 6.1 | 18.9 |
| 17 | 996230 | not present | - | not present | i/v and oral antibiotics | inj Amikacin , Oral Azee | 4 | Not vaccinated for typhoid | pallor + | not present | not present | 130 | 100 | 60 | 97.8 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 8.9 | 70.4 |
| 18 | 748178 | present | vomitings x 1 day , 3 episodes per day , non bilious , non projectile | not present | oral antibiotics | Cefixime | 2 | Not vaccinated for typhoid | pallor + | not present | not present | 116 | 100 | 60 | 97.4 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | liver 3 cm palpable below RCM , spleen non palpable | 15 | 10 | 70.5 |
| 19 | 997791 | not present | - | not present | oral antibiotics | cefixime | 4 | Not vaccinated for typhoid | pallor + | not present | not present | 160 | 100 | 70 | 97 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | liver 3 cm palpable below RCM , spleen non palpable | 15 | 9.9 | 76.6 |
| 20 | 1004088 | present | vomitings present , 14 days back , for 2 days , non bilious , non projectile | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 112 | 110 | 70 | 104 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | liver 3 cm palpable below RCM , spleen non palpable | 15 | 10.7 | 80.5 |
| 21 | 1005164 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 102 | 110 | 70 | 99 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | liver 3 cm palpable below RCM , spleen tip palpable | 15 | 11.4 | 35.9 |
| 22 | 1006828 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 120 | 126 | 92 | 101 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 2 cm below RCM , spleen non palpable | 15 | 9.6 | 31.9 |
| 23 | 1007436 | present | vomitings x 2 days , non projectile , non bilious | altered sensorium + | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 90 | 100 | 70 | 99 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | liver 3 cm palpable below RCM , spleen non palpable | 14 | 9.3 | 74.6 |
| 24 | 3624 | not present | - | not present | oral antibiotics | Cefixime | 2 | Not vaccinated for typhoid | pallor + | not present | not present | 90 | 118 | 80 | 99 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | liver 3 cm palpable below RCM , spleen tip palpable | 15 | 12.3 | 38.8 |
| 25 | 1009264 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 132 | 126 | 74 | 102 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 4 cm below RCM , spleen not palpable | 15 | 13.5 | 80.5 |
| 26 | 1009172 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 122 | 117 | 80 | 101 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | liver 4 cm palpable below RCM , spleen 5 cm below LCM | 15 | 5.6 | 77 |
| 27 | 1011789 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 128 | 120 | 80 | 100 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | liver 3 cm palpable below RCM , spleen non palpable | 15 | 11.7 | 79.5 |
| 28 | 1011696 | present | loose stools + , 4 episodes per day , non blood stained | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 168 | 90 | 60 | 102.3 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | liver 3 cm palpable below RCM , spleen non palpable | 15 | 8 | 70.4 |
| 29 | 1020943 | not present | - | altered sensorium + | i/v antibiotics | inj Vancomycin and inj . ceftriaxone | 3 | Not vaccinated for typhoid | pallor + | not present | not present | 110 | 110 | 70 | 100.8 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 10 | 10.2 | 90.5 |
| 30 | 1021465 | present | vomitings x 2 days , non projectile , non bilious | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 139 | 90 | 50 | 102.6 | 3 | b/l air entry + , reduced at bases | S1 , S2 normal , no murmur | Liver palpable 3 cm below RCM, spleen non palpable | 15 | 6.9 | 63 |
| 31 | 999472 | present | vomitings x 2 days , non projectile , non bilious | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 154 | 100 | 60 | 99 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 11.1 | 70.4 |
| 32 | 1025398 | not present | - | not present | oral antibiotics | cefixime | 2 | Not vaccinated for typhoid | pallor + | not present | not present | 130 | 90 | 50 | 98.2 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 2 cm below RCM , spleen non palpable | 15 | 11.5 | 34.3 |
| 33 | 127767 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 118 | 110 | 80 | 98.2 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 2 cm below RCM , spleen non palpable | 15 | 12.1 | 90.6 |

| Sr. No | MRD | Anemia | TLC | N | L | M | E | Platelets | CRPq | ESR | LDH | SGOT | SGPT | ALP | TO | TH | AH | BH | Blood Culture | Azithromycin | cotrimoxazole | Ceftriaxone | Ciprofloxacin | Ofloxacin | Ampicillin | Cefixime | Cefuroxime | Chloramphenicol | Cefotaxime |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 16 | 9911963 | severe | 5500 | 79.8 | 13.2 | 6.3 | 0.3 | - | 22.8 | 120 | 994 | - | - | - | 320 | 80 | <20 | nil | no growth | - | - | - | - | - | - | - | - | - | - |
| 17 | 996230 | moderate | 13000 | 39.3 | 49.4 | 10.2 | 0.7 | 577000 | 8.29 | - | 351 | - | - | - | 320 ET | nil | nil | nil | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 18 | 748178 | Mild | 4700 | 59 | 35.7 | 4.9 | 0.1 | 361000 | 72.9 | - | 401 | - | - | - | <20 | 320 ET | <20 | nil | salmonella typhi | S | S | S | R | S | R | S | R | S | - |
| 19 | 997791 | moderate | 7100 | 65.7 | 27 | 6.7 | 0 | 156000 | 42.7 | 22 | - | 158 | 71 | - | 320 ET | 320 ET | <20 | nil | salmonella typhi | S | S | S | S | S | S | S | R | S | - |
| 20 | 1004088 | Mild | 8900 | 48.8 | 40.4 | 10 | 0 | 370000 | 64.08 | - | - | 59 | 75 | - | 160 | 160 | <20 | nil | no growth | - | - | - | - | - | - | - | - | - | - |
| 21 | 1005164 | Mild | 6000 | 66.2 | 26.7 | 6.8 | 0 | 221000 | 115.2 | - | 468 | 96 | 100 | - | 80 | 20 | 160 | nil | salmonella parayphiA | S | S | S | R | S | R | S | R | S | - |
| 22 | 1006828 | moderate | 5900 | 53 | 35 | 10.7 | 0.3 | 305000 | 20.03 | - | - | 45 | 39 | - | 320 | 160 | <20 | nil | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 23 | 1007436 | moderate | 1200 | 84.2 | 10.7 | 5 | 0.1 | 22000 | 54 | 30 | - | - | 151 | 29 | 160 | 640ET | <20 | nil | no growth | - | - | - | - | - | - | - | - | - | - |
| 24 | 3624 | Mild | 13200 | 55 | 38 | 4.8 | 1.3 | 462000 | 13 | 32 | 224 | 34 | 20 | - | - | - | - | - | salmonella parayphiA | S | S | S | R | S | S | S | R | S | - |
| 25 | 1009264 | Mild | 5000 | 62 | 32.5 | 5.2 | 0 | 82000 | 78 | 25 | 448 | 181 | 138 | - | 40 | 20 | 320ET | nil | salmonella parayphiA | S | S | S | R | S | R | S | R | S | - |
| 26 | 1009172 | severe | 2700 | 25 | 50 | 3 | 0 | 12000 | - | - | 326 | - | - | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 27 | 1011789 | Mild | 5000 | 64.3 | 32.2 | 3.2 | 0 | 150000 | 65 | 45 | - | 61 | 33 | - | 80 | 320 ET | <20 | nil | no growth | - | - | - | - | - | - | - | - | - | - |
| 28 | 1011696 | moderate | 10400 | 80 | 18 | 2 | 0 | 317000 | 36 | 80 | - | 217 | 229 | - | 80 | 640ET | <20 | nil | no growth | - | - | - | - | - | - | - | - | - | - |
| 29 | 1020943 | Mild | 6800 | 80 | 15 | 4 | 1 | 94000 | 52 | 60 | 482 | 96 | 88 | 814 | 80 | 2560 ET | 80 | nil | no growth | - | - | - | - | - | - | - | - | - | - |
| 30 | 1021465 | moderate | 5700 | 60.3 | 27 | 11 | 0 | 20000 | 166 | 20 | 951 | 374 | 124 | 485 | <20 | 20 | 320ET | nil | salmonella parayphiA | S | S | S | R | S | S | S | R | S | - |
| 31 | 999472 | Mild | 8300 | 70.3 | 18.9 | 10.4 | 0 | 293000 | 234.3 | - | - | - | - | - | 40 | 80 | <20 | nil | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 32 | 1025398 | Mild | 8400 | 27.9 | 47 | 10 | 14 | 258000 | 0.96 | - | 402 | 104 | 60 | - | 160 | 40 | <20 | nil | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 33 | 127767 | Mild | 5200 | 69.2 | 25.5 | 5 | 0 | 164000 | 63 | - | - | - | - | - | 160 | 320 ET | <20 | nil | salmonella typhi | S | S | S | R | S | S | S | R | S | - |

| Sr. No | MRD | Duration | Cefepime tazobactum | Duration | Ceftriaxone | Duration | Ofloxacin | Duration | Ciprofloxacin | Duration | Aminoglycosides | Duration Of antibiotics Intake | Antibiotics | No of Antibiotics | Days of Deffervesence of Fever | Deffervesence of Fever group | Outcome | FINAL DIAGNOSIS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 16 | 9911963 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 10 | 2 | Discharge | Enteric Fever |
| 17 | 996230 | - | - | - | Inj Ceftriaxone | 4 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 13 | 2 | Discharge | Typhoid Fever |
| 18 | 748178 | - | - | - | Inj Ceftriaxone | 5 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 11 | 2 | Discharge | Typhoid Fever |
| 19 | 997791 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 8 | 1 | Discharge | Typhoid Fever |
| 20 | 1004088 | - | i/v actamase | 7 days | - | - | - | - | - | - | oral azithromycin | 5 days | i/v actamase,oral azithromycin | Double | 15 | 2 | Discharge | Enteric Fever |
| 21 | 1005164 | - | - | - | Inj Ceftriaxone | 3 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 7 | 1 | Discharge | Paratyphoid Fever |
| 22 | 1006828 | - | - | - | Inj Ceftriaxone | 9 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 11 | 2 | Discharge | Infarct in internal capsule region with Typhoid Fever |
| 23 | 1007436 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | oral azithromycin | 5 days | Inj Ceftriaxone,oral azithromycin | Double | 11 | 2 | Discharge | Enteric Fever |
| 24 | 3624 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 11 | 2 | Discharge | Paratyphoid Fever |
| 25 | 1009264 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | oral azithromycin | 5 days | Inj Ceftriaxone,oral azithromycin | Double | 10 | 2 | Diischarge | Paratyphoid Fever |
| 26 | 1009172 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 5 | 1 | Diischarge | Typhoid Fever with Bcell ALL |
| 27 | 1011789 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 13 | 2 | Diischarge | Enteric Fever |
| 28 | 1011696 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | oral azithromycin | 5 days | Inj Ceftriaxone,oral azithromycin | Double | 13 | 2 | Discharge | Enteric Fever |
| 29 | 1020943 | - | - | - | Inj Ceftriaxone | 1 day | - | - | - | - | - | - | Inj Ceftriaxone | Single | - | - | DOR | complicated Typhoid Fever with Encephalopathy with Thrombocytopenia |
| 30 | 1021465 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | oral azithromycin | 5 days | Inj Ceftriaxone,oral azithromycin | Double | 14 | 2 | Discharge | Complicated Paratyphoid fever with Right Pleural Effusion with Thrombocytopenia with Anemia |
| 31 | 999472 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 11 | 2 | Discharge | Typhoid Fever with F/I/C/O cerebellar Atrophy with Developmental Delay |
| 32 | 1025398 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 14 | 2 | Diischarge | Typhoid Fever |
| 33 | 127767 | - | - | - | i/v ceftriaxone, oral cefixime | i/v for 7 days, oral for 7 days | - | - | - | - | - | - | i/v ceftriaxone, oral cefixime | Double | 8 | 1 | Diischarge | Typhoid Fever |

| Sr. No | MRD | Age (months ) | Sex | DOA | DOD | Hospital stay ( days ) | Actual Weight (Kg) | Actual Height/ Length(cm) | Actual Head Circumference (cm) | Actual BMI | Expected Weight (Kg) | Expected Height/ Length(cm) | Expected Head Circumference (cm) | Expected BMI | Fever Duration ( days ) | Onset | Grade | Type | Rigors/Chill | Pain Abdomen | Characteristics of Pain Abdomen |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 34 | 574317 | 48 | male | 24-02-2021 | 28-02-2021 | 5 | 15 | 101.5 | 49 | 14.7 | 15.5 | 106 | 50.5 | 13.8 | 7 | acute | moderate | intermittent | not present | present | 7 days , mild in epigastrium , non radiating ,no aggravating / relieving factor |
| 35 | 1035440 | 144 | female | 26-02-2021 | 02-03-2021 | 5 | 64 | 155 | 50 | 26.6 | 40 | 150 | 50 | 16 | 9 | acute | moderate | intermittent | not present | present | mild , in epigastrium , no aggravating, relieving factors |
| 36 | 262527 | 70 | male | 20-03-2021 | 27-03-2021 | 4 | 22.6 | 116 | 53.5 | 16.8 | 18.2 | 111.9 | 50.7 | 14.8 | 4 | acute | moderate | intermittent | not present | present | 1 day , in epigastrium , mild , non radiating , no aggravting relieving factors |
| 37 | 1066517 | 96 | female | 29-03-2021 | 04-04-2021 | 8 | 32 | 125 | - | 20.5 | 24 | 125.4 | - | 15.3 | 5 | acute | moderate | intermittent | not present | present | mild , in epigastrium , no aggravating, relieving factors |
| 38 | 1085186 | 48 | female | 13-04-2021 | 22-04-2021 | 4 | 14 | 105 | 47 | - | 16.1 | 102.7 | 49 | - | 4 | acute | moderate | intermittent | present | present | mild , in epigastrium , no aggravating, relieving factors |
| 39 | 1070567 | 180 | male | 01-04-2021 | 08-04-2021 | 8 | 43 | 167 | - | 15.4 | 53 | 165 | - | 19.2 | 30 | insidious | moderate | intermittent | not present | present | mild , in epigastrium , no aggravating, relieving factors |
| 40 | 920216 | 36 | female | 24-03-2021 | 31-03-2021 | 8 | 15 | 97 | 49.5 | - | 14.5 | 96 | 49 | - | 6 | acute | moderate | intermittent | not present | not present | - |
| 41 | 1079987 | 156 | male | 08-04-2021 | 14-04-2021 | 7 | 44 | 160 | - | 17.1 | 43.3 | 160 | - | 17.1 | 7 | acute | moderate | intermittent | not present | not present | - |
| 42 | 877434 | 15 | male | 23-02-2021 | 25-02-2021 | 3 | 11 | 78 | 48 | - | 10 | 78 | 46.5 | - | 7 | acute | high | intermittent | not present | not present | - |
| 43 | 773419 | 24 | male | 15-04-2021 | 18-04-2021 | 4 | 11 | 80 | 49 | 17.1 | 11.5 | 86.4 | 47. 2 | 15.7 | 7 | acute | high | intermittent | not present | not present | - |
| 44 | 3747 | 156 | female | 17-05-2021 | 21-05-2021 | 5 | 50 | 157 | - | 20.28 | 46 | 156 | - | 19.2 | 10 | insidious | moderate | intermittent | not present | not present | - |
| 45 | 1111460 | 36 | female | 21-05-2021 | 29-05-2021 | 9 | 8 | 83 | 46 | 11.7 | 14 | 95 | 48 .5 | 15.5 | 2 | acute | moderate | intermittent | not present | not present | - |
| 46 | 1113191 | 12 | female | 25-05-2021 | 04-06-2021 | 6 | 9.3 | 81 | 45 | - | 9 | 80 | - | - | 6 | acute | high | intermittent | not present | not present | - |
| 47 | 25894 | 60 | female | 28-05-2021 | 03-06-2021 | 7 | 18.2 | 118 | - | 13.09 | 16.4 | 110 | 45 | 14.4 | 7 | acute | high | intermittent | not present | not present | - |
| 48 | 1114926 | 84 | male | 29-05-2021 | 06-06-2021 | 6 | 7.6 | 71 | 45.5 | - | 8 | 67 | 43 | - | 6 | acute | moderate | intermittent | not present | not present | - |
| 49 | 1113877 | 12 | male | 29-05-2021 | 05-06-2021 | 8 | 10.8 | 80 | 47.5 | - | 9.9 | 76 | 46.3 | - | 5 | acute | moderate | intermittent | not present | not present | - |

| Sr. No | MRD | Loose Stools / Vomitings | Loose stools /Vomitings EPISODES | Unconsciousness /Seizures | Past Drug History | Type of Antibiotic taken | Duration of Antibiotic | Vaccination History | Anaemia | Icterus | Edema: Face /Feet | HR | SBP | DBP | Temp | CFT | Chest | CVS | Liver /Spleen /Ascites | AVPU / GCS | Hb | MCV |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 34 | 574317 | present | vomitings x 7 days , 2 episodes / day, non projectile , non bilious , non blood stained | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 108 | 120 | 70 | 98.2 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver palpable 4 cm below RCM , spleen non palpable | 15 | 10.9 | 80 |
| 35 | 1035440 | present | one episode of vomitings , non projectile , non bilious | not present | no h/o previous antibiotic intake | - | - | 1 dose of typhoid vaccine , conjugated recieved . | pallor + | not present | not present | 80 | 110 | 70 | 98.2 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 4cm below RCM , spleen 2 cm below LCM , No ascites | 15 | 9.9 | 79.6 |
| 36 | 262527 | present | vomitings x 2 days , 3 - 4 episodes per day , non bilious , non projectile , non blood stained . | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 136 | 120 | 70 | 99 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 5 cm below RCM , spleen tip palpable | 15 | 10.2 | 75 |
| 37 | 1066517 | present | vomitings x 4 days , non bilious , non projectile , 3 - 4 episodes / day ;non blood stained . | not present | oral antibiotics | cefixime | 3 | Not vaccinated for typhoid | pallor + | not present | not present | 102 | 110 | 60 | 99 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 2 cm below RCM , spleen tip palpable | 15 | 11.8 | 79 |
| 38 | 1085186 | present | vomitings x 1 day , 3 episodes per day , non bilious , non projectile | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 142 | 110 | 70 | 102 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 3 cm below RCM , spleen not palpable | 15 | 9.9 | 80.8 |
| 39 | 1070567 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 92 | 120 | 8 | 99 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 2 cm below RCM , spleen non palpable | 15 | 12.5 | 84 |
| 40 | 920216 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 120 | 100 | 60 | 99 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 4 cm below RCM , spleen non palpable | 15 | 9 | 64.5 |
| 41 | 1079987 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 104 | 120 | 80 | 99 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver palpable 4 cm below RCM , spleen non palpable | 15 | 12.9 | 81.2 |
| 42 | 877434 | not present | - | not present | oral antibiotics | oral cefixime | 8 | Not vaccinated for typhoid | pallor + | not present | not present | 110 | 100 | 60 | 99 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | liver 3 cm palpable below RCM , spleen non palpable | 15 | 12.6 | 76.9 |
| 43 | 773419 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 118 | 90 | 60 | 104 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 3 cm below RCM , spleen non palpable | 15 | 5.9 | 48.5 |
| 44 | 3747 | not present | - | not present | on antiepileptic medications | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 106 | 110 | 80 | 98.4 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 11.2 | 82.4 |
| 45 | 1111460 | present | Vomitings , x 2 days , acute , 2 -3 episodes per day , non bilious , non projectile , watery , non blood stained | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 134 | 100 | 60 | 100.4 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 6.1 | 56 |
| 46 | 1113191 | present | Loose stools x 4 days , 10 - 12 stools / day , greenish , non blood stained | not present | oral azithromycin | azithromycin | 2 | Not vaccinated for typhoid | pallor + | not present | not present | 164 | 118 | 79 | 103 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 3 cm below RCM , spleen non palpable | 15 | 9.8 | 75.7 |
| 47 | 25894 | not present | - | not present | oral antibiotics | oral cefixime | 2 | Not vaccinated for typhoid | pallor + | not present | not present | 120 | 92 | 60 | 97 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 3 cm below RCM , spleen non palpable | 15 | 13.8 | 84 |
| 48 | 1114926 | not present | - | not present | oral antibiotics | cepodem , cefixime | 4 cepodem , 1 day taxim O | Not vaccinated for typhoid | pallor + | not present | not present | 150 | 70 | 50 | 102.5 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 2 cm below RCM , spleen non palpable | 15 | 10.5 | 75.9 |
| 49 | 1113877 | present | loose stoolsx 4 days , 3 - 4 episodes per day , greenish , non blood stained | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 148 | 100 | 60 | 101.4 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 9.7 | 29.9 |

| Sr. No | MRD | Anemia | TLC | N | L | M | E | Platelets | CRPq | ESR | LDH | SGOT | SGPT | ALP | TO | TH | AH | BH | Blood Culture | Azithromycin | cotrimoxazole | Ceftriaxone | Ciprofloxacin | Ofloxacin | Ampicillin | Cefixime | Cefuroxime | Chloramphenicol | Cefotaxime |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 34 | 574317 | Mild | 9600 | 47 | 46 | 5 | 0.1 | 309000 | 10.5 | - | 549 | 123 | 86 | - | <20 | 320 ET | <20 | nil | no growth | - | - | - | - | - | - | - | - | - | - |
| 35 | 1035440 | moderate | 6700 | 74 | 19 | 5.8 | 0.1 | 171000 | 102 | - | 856 | 101 | 79 | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 36 | 262527 | Mild | 6500 | 45 | 45 | 8 | 0.2 | 249000 | 141 | 16 | 617 | 220 | 122 | - | <20 | 20 | 320ET | nil | salmonella parayphiA | S | S | S | R | S | S | S | R | S | - |
| 37 | 1066517 | Mild | 10500 | 82 | 13 | 4.7 | 0 | 313000 | 70.2 | - | 536 | 102 | 70 | - | <20 | 20 | <20 | nil | salmonella typhi | S | S | S | R | S | S | S | S | S | - |
| 38 | 1085186 | moderate | 3800 | 51 | 41 | 6.8 | 0 | 125000 | 141 | - | 369 | 62 | 36 | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 39 | 1070567 | Mild | 6900 | 39 | 48 | 10.5 | 1.6 | 228000 | 50.4 | - | 407 | - | - | - | 40 | 80 | <20 | nil | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 40 | 920216 | moderate | 7400 | 50.6 | 45.5 | 3.7 | 0 | 237000 | - | - | 417 | 50 | 30 | - | 640 ET | 320 ET | <20 | nil | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 41 | 1079987 | 6.7 | 6.7 | 67.1 | 25.6 | 7.1 | 0 | 182000 | 114 | - | 395 | 75 | - | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 42 | 877434 | Mild | 10000 | 48 | 41 | 10 | 0 | 212000 | 16.2 | - | - | - | - | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | S | S | - |
| 43 | 773419 | severe | 13800 | 41 | 50 | 7.9 | 0.2 | 270000 | 38.2 | - | - | - | - | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 44 | 3747 | Mild | 6200 | 48 | 40 | 10.5 | 0.1 | 206000 | 91 | - | - | 75 | 81 | 126 | - | - | - | - | salmonella parayphiA | S | S | S | R | S | S | S | R | S | - |
| 45 | 1111460 | severe | 9900 | 58 | 37 | 3.5 | 0 | 167000 | 116 | 10 | - | 74 | 31 | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 46 | 1113191 | moderate | 11100 | 81 | 11 | 7.1 | 0 | 52000 | 174 | - | 676 | 89 | 39 | 296 | 320 ET | 2560 ET | <20 | nil | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 47 | 25894 | Mild | 6100 | 42.1 | 48 | 9.2 | 0.1 | 261000 | 66 | - | 439 | 80 | 60 | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 48 | 1114926 | Mild | 11700 | 48 | 43 | 6 | 0.4 | 283000 | 34 | - | 447 | 70 | 76 | - | - | - | - | - | salmonella typhi | S | S | S | S | S | S | S | S | S | - |
| 49 | 1113877 | moderate | 10100 | 56.6 | 32.6 | 10.5 | 0 | 150000 | 91 | - | 387 | 88 | 53 | - | <20 | 40 | <20 | nil | salmonella typhi | S | S | S | R | S | S | S | R | S | - |

| Sr. No | MRD | Duration | Cefepime tazobactum | Duration | Ceftriaxone | Duration | Ofloxacin | Duration | Ciprofloxacin | Duration | Aminoglycosides | Duration Of antibiotics Intake | Antibiotics | No of Antibiotics | Days of Deffervesence of Fever | Deffervesence of Fever group | Outcome | FINAL DIAGNOSIS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 34 | 574317 | - | - | - | Inj Ceftriaxone | 5 days, oral cefixime | - | - | - | - | - | - | Inj Ceftriaxone | Single | 8 | 1 | Discharge | Enteric Fever |
| 35 | 1035440 | - | - | - | i/v ceftriaxone, oral cefixime | i/v 5 days , oral 9 days | - | - | - | - | - | - | i/v ceftriaxone, oral cefixime | Double | 4 | 1 | Diischarge | Typhoid Fever with Obesity |
| 36 | 262527 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 11 | 2 | Discharge | Paratyphoid Fever |
| 37 | 1066517 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 12 | 2 | Discharge | Typhoid Fever |
| 38 | 1085186 | - | - | - | Inj Ceftriaxone | 10 days | - | - | - | - | oral azithromycin | 8 days | Inj Ceftriaxone,oral azithromycin | Double | 12 | 2 | Discharge | Typhoid Fever |
| 39 | 1070567 | - | - | - | i/v ceftriaxone, oral cefixime | 7 days | - | - | - | - | - | - | i/v ceftriaxone, oral cefixime | Double | 6 | 1 | Discharge | Typhoid Fever |
| 40 | 920216 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 12 | 2 | Discharge | Typhoid Fever |
| 41 | 1079987 | - | - | - | Inj Ceftriaxone | 8 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 13 | 2 | Discharge | Typhoid Fever |
| 42 | 877434 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 12 | 2 | Diischarge | Typhoid Fever |
| 43 | 773419 | - | - | - | Inj Ceftriaxone | 3 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 9 | 1 | Diischarge | Typhoid Fever |
| 44 | 3747 | - | - | - | Inj Ceftriaxone | 5 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 12 | 2 | Discharge | Paratyphoid fever with VSD with Vitamin D Deficiency |
| 45 | 1111460 | - | - | - | Inj Ceftriaxone | 8 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 5 | 1 | Discharge | Typhoid Fever with Failure To Thrive |
| 46 | 1113191 | - | - | - | i/v ceftriaxone , oral azithromycin | 9 days | - | - | - | - | - | - | i/v ceftriaxone , oral azithromycin | Double | 13 | 2 | Discharge | Typhoid Fever with Acute Diarrheal Disease with some dehydration |
| 47 | 25894 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 12 | 2 | Discharge | Typhoid Fever |
| 48 | 1114926 | - | - | - | Inj Ceftriaxone | 9 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 13 | 2 | Diischarge | Typhoid Fever |
| 49 | 1113877 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 10 | 2 | Discharge | Typhoid Fever |

| Sr. No | MRD | Age (months ) | Sex | DOA | DOD | Hospital stay ( days ) | Actual Weight (Kg) | Actual Height/ Length(cm) | Actual Head Circumference (cm) | Actual BMI | Expected Weight (Kg) | Expected Height/ Length(cm) | Expected Head Circumference (cm) | Expected BMI | Fever Duration ( days ) | Onset | Grade | Type | Rigors/Chill | Pain Abdomen | Characteristics of Pain Abdomen |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 50 | 1020888 | 12 | female | 19-02-2021 | 25-02-2021 | 6 | 9.5 | 75 | 46 | - | 9 | 74 | 45 | - | 2 | acute | high | intermittent | not present | not present | - |
| 51 | 1131444 | 20 | female | 03-07-2021 | 10-07-2021 | 5 | 9.2 | 80 | 45 | - | 10 | 82 | 46 | - | 5 | acute | high | intermittent | present | not present | - |
| 52 | 701113 | 29 | male | 04-07-2021 | 10-07-2021 | 5 | 10 | 88 | 49 | - | 13 | 90 | 47.2 | - | 5 | acute | high | intermittent | not present | not present | - |
| 53 | 1131562 | 96 | male | 07-07-2021 | 13-07-2021 | 1 | 25 | 126 | - | 14 | 24 | 124 | - | 15 | 7 | acute | high | intermittent | not present | present | mild at right hypochondrium , x 1 day |
| 54 | 1137283 | 144 | male | 17-07-2021 | 21-07-2021 | 5 | 30 | 138 | - | 15.7 | 48 | 152 | - | 16 | 8 | acute | high | intermittent | not present | present | acute in onset , non radiating , no aggravating releiving factors |
| 55 | 1137643 | 84 | male | 17-07-2021 | 27-07-2021 | 11 | 20 | 122 | - | 13.4 | 22 | 123 | - | 14.8 | 6 | acute | high | intermittent | not present | not present | - |
| 56 | 1139373 | 120 | female | 21-07-2021 | 26 / 07 2021 | 6 | 23.2 | 136 | - | 12.6 | 32 | 140 | - | 16.4 | 6 | acute | high | intermittent | not present | not present | - |
| 57 | 1141552 | 132 | female | 25-07-2021 | 02-08-2021 | 9 | 37 | 153 | - | 15.1 | 37.5 | 148 | - | 16 | 5 | acute | high | intermittent | not present | not present | - |
| 58 | 218372 | 56 | male | 26-07-2021 | 02-08-2021 | 8 | 16 | 110 | 52 | - | 17 | 106 | 52 | - | 3 | acute | high | intermittent | not present | not present | - |
| 59 | 1144894 | 12 | male | 29-07-2021 | 04-08-2021 | 7 | 11 | 85 | 47 | - | 11.5 | 85 | 47 | - | 10 | acute | moderate | intermittent | not present | not present | - |
| 60 | 1138164 | 108 | female | 16-07-2021 | 26-07-2021 | 11 | 25 | 123 | - | 16.5 | 27 | 133 | - | 15.2 | 5 | acute | high | intermittent | not present | present | mild , since 5 days epigastric , non radiating , no aggravating releiving factors |
| 61 | 721137 | 144 | male | 13-07-2021 | 19-07-2021 | 7 | 44 | 152 | - | 19.13 | 40 | 150 | - | 18 | 3 | acute | high | intermittent | not present | not present | - |
| 62 | 1135839 | 156 | male | 12-07-2021 | 19-07-2021 | 8 | 52 | 154 | - | 22 | 44 | 154 | - | 18.6 | 7 | acute | moderate | intermittent | present | not present | - |
| 63 | 1134515 | 10 | female | 10-07-2021 | 14-07-2021 | 5 | 7.6 | 70 | 43 | - | 8 | 67 | 43 | - | 9 | acute | high | intermittent | not present | not present | - |

| Sr. No | MRD | Loose Stools / Vomitings | Loose stools /Vomitings EPISODES | Unconsciousness /Seizures | Past Drug History | Type of Antibiotic taken | Duration of Antibiotic | Vaccination History | Anaemia | Icterus | Edema: Face /Feet | HR | SBP | DBP | Temp | CFT | Chest | CVS | Liver /Spleen /Ascites | AVPU / GCS | Hb | MCV |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 50 | 1020888 | present | loose stools x 2 days , 4 - 5 episodes per day , greenish , non blood stained | episode of uprolling of eye | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 160 | 90 | 60 | 101.8 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 7.7 | 60.4 |
| 51 | 1131444 | present | Loose stools x 2 days , 2 - 3 episodes / day ; Vomitings x 1 day , non projectile , non bilious | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 148 | 90 | 60 | 101.3 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 8.5 | 50.3 |
| 52 | 701113 | present | loose stools x 5 days , 6 - 7 episodes per day , greenish , non projectile | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 150 | 108 | 64 | 102 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 7.5 | 54.9 |
| 53 | 1131562 | not present | - | not present | oral cefixime x 2 days | Cefixime | 2 | Not vaccinated for typhoid | pallor + | not present | not present | 110 | 116 | 76 | 102.3 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver palpable 3 cm below RCM , Spleen palpable 1 cm below LCM | 15 | 9.9 | 79 |
| 54 | 1137283 | present | loose stools x 3 days , 3 - 4 episodes / day , watery , non blood stained | not present | present | oral cefixime | 2 | Not vaccinated for typhoid | pallor + | not present | not present | 120 | 110 | 60 | 99 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 2 cm below RCM , spleen non palpable | 15 | 12.4 | 35.8 |
| 55 | 1137643 | present | Loose stools x 2 days , watery , non blood stained | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 100 | 98 | 60 | 101 | 2 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 3 cm below RCM , spleen non palpable | 15 | 11.4 | 35.5 |
| 56 | 1139373 | not present | - | not present | no h/o previous antibiotic intake | - | 2 | Not vaccinated for typhoid | pallor + | not present | not present | 120 | 110 | 60 | 101.3 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 2 cm below RCM , spleen tip palpable | 15 | 10.7 | 32.4 |
| 57 | 1141552 | present | loose stools x 2 days , 4 - 5 episodes / day , non blood stained , not associated with meals ; Vomitings x 2 days , 3 - 4 episodes / day , non bilious , non projectile , non blood stained | not present | present | oral cefixime | 2 | Not vaccinated for typhoid | pallor + | not present | not present | 128 | 100 | 60 | 102.6 | 2 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 2 cm below RCM , spleen non palpable | 15 | 13.5 | 39.8 |
| 58 | 218372 | present | Vomitings x 1 day , non bilious , non projectile , nn blood stained | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 112 | 90 | 60 | 101.3 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver , spleen non palpable | 15 | 9.8 | 32.2 |
| 59 | 1144894 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 140 | 90 | 60 | 101.4 | 2 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 2 cm below RCM , spleen tip palpable | 15 | 6.8 | 23.9 |
| 60 | 1138164 | present | present since 5 days , 2 - 3 episodes , non bilious , non projectile , non blood stained , loose stools x 5 days , watery , non blood stained | not present | present | Cefixime | 1 | Not vaccinated for typhoid | pallor + | not present | not present | 110 | 120 | 62 | 101.3 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 4 cm below RCM , spleen 3 cm palpable below LCM | 15 | 11.3 | 36.6 |
| 61 | 721137 | not present | - | not present | oral cefixime x 2 days | Cefixime | 1 | Not vaccinated for typhoid | pallor + | not present | not present | 98 | 122 | 62 | 100.8 | 2 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 4 cm below RCM , spleen tip palpable | 15 | 12.9 | 39.8 |
| 62 | 1135839 | present | loose stools x 2 day , 4 - 5 episodes / day , non blood stained, not associated with vomitings | not present | oral cefixime x 2 days | Cefixime | 2 | Not vaccinated for typhoid | pallor + | not present | not present | 110 | 120 | 62 | 101.4 | 2 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | liver 3 cm palpable below RCM , spleen tip palpable | 15 | 12.9 | 41.4 |
| 63 | 1134515 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 134 | 90 | 60 | 102.2 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | - | 15 | 10.2 | 32.5 |

| Sr. No | MRD | Anemia | TLC | N | L | M | E | Platelets | CRPq | ESR | LDH | SGOT | SGPT | ALP | TO | TH | AH | BH | Blood Culture | Azithromycin | cotrimoxazole | Ceftriaxone | Ciprofloxacin | Ofloxacin | Ampicillin | Cefixime | Cefuroxime | Chloramphenicol | Cefotaxime |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 50 | 1020888 | moderate | 3600 | 30 | 60 | 8 | 2 | 279000 | 95 | - | - | - | - | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 51 | 1131444 | moderate | 4000 | 12.8 | 81.8 | 4.8 | 0.1 | 198000 | 36.18 | - | 805 | 123 | 94 | - | - | - | - | - | salmonella typhi | S | S | S | R | R | S | S | S | S | - |
| 52 | 701113 | moderate | 8000 | 80 | 9.6 | 10 | 0.1 | 160000 | 69.2 | 42 | 433 | 51 | 45 | - | 320 | 2560 ET | <20 | nil | salmonella typhi | S | S | S | S | S | S | S | S | S | - |
| 53 | 1131562 | Mild | 8400 | 43 | 44 | 11.6 | 0.1 | 182000 | 120 | - | 560 | 149 | 115 | - | - | - | - | - | salmonella typhi | S | S | S | R | R | S | R | R | S | - |
| 54 | 1137283 | Mild | 4100 | 69 | 22 | 7 | 0.1 | 150000 | 113 | - | 856 | 117 | 77 | - | <20 | 160 | <20 | nil | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 55 | 1137643 | Mild | 10300 | 70 | 24.7 | 5 | 0 | 150000 | 49.5 | - | 1334 | 115 | 74 | - | 40 | 320 ET | <20 | 0 | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 56 | 1139373 | Mild | 7500 | 61.5 | 32 | 6.2 | 0 | 180000 | 80.1 | - | 576 | 139 | 138 | - | 40 | 20 | <20 | nil | salmonella typhi | S | S | S | R | R | S | S | R | S | - |
| 57 | 1141552 | Mild | 7700 | 62.5 | 26.3 | 11.1 | 0 | 210000 | 58.1 | 30 | 364 | 48 | 39 | - | 40 | 20 | <20 | nil | salmonella typhi | S | S | S | R | R | S | S | R | S | - |
| 58 | 218372 | Mild | 9200 | 76 | 19 | 4.1 | 0 | 246000 | 30.8 | 8 | 643 | 177 | 115 | - | 40 | 40 | 640ET | -59 | salmonella parayphiA | S | S | S | R | R | S | S | R | S | - |
| 59 | 1144894 | moderate | 7400 | 40 | 50 | 8 | 2 | 152000 | 47 | - | 675 | 84 | 50 | - | <20 | 320 HT | <20 | nil | salmonella typhi | S | S | S | R | R | S | S | R | S | - |
| 60 | 1138164 | Mild | 6300 | 57 | 36 | 5.7 | 0.1 | 50000 | 84 | - | 738 | 209 | 149 | - | - | - | - | - | salmonella parayphiA | S | S | S | R | S | S | S | R | S | - |
| 61 | 721137 | Mild | 4000 | 51 | 36.1 | 12.7 | 0 | 178000 | 29.4 | - | 413 | 60 | 32 | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 62 | 1135839 | Mild | 7700 | 63 | 29 | 6.8 | 0 | 260000 | 88 | - | - | 59 | 41 | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 63 | 1134515 | Mild | 17800 | 40 | 49 | 9.7 | 0.6 | 668000 | 55.5 | - | 392 | 35 | 23 | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |

| Sr. No | MRD | Duration | Cefepime tazobactum | Duration | Ceftriaxone | Duration | Ofloxacin | Duration | Ciprofloxacin | Duration | Aminoglycosides | Duration Of antibiotics Intake | Antibiotics | No of Antibiotics | Days of Deffervesence of Fever | Deffervesence of Fever group | Outcome | FINAL DIAGNOSIS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 50 | 1020888 | - | - | - | Inj Ceftriaxone | 5 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 7 | 1 | Discharge | Typhoid Fever with Typical Febrile Seizures |
| 51 | 1131444 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | oral azithromycin | 5 days | Inj Ceftriaxone,oral azithromycin | Double | 12 | 2 | Discharge | Typhoid Fever |
| 52 | 701113 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 11 | 2 | Discharge | Typhoid Fever |
| 53 | 1131562 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 12 | 2 | Discharge | Typhoid Fever |
| 54 | 1137283 | - | - | - | Inj Ceftriaxone | 5 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 11 | 2 | Discharge | Typhoid Fever |
| 55 | 1137643 | - | - | - | Inj Ceftriaxone | 8 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 14 | 2 | Discharge | Typhoid Fever |
| 56 | 1139373 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 9 | 1 | Discharge | Typhoid Fever |
| 57 | 1141552 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 10 | 2 | Discharge | Typhoid Fever |
| 58 | 218372 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 8 | 1 | Discharge | Paratyphoid Fever |
| 59 | 1144894 | - | - | - | Inj Ceftriaxone | 8 days | - | - | - | - | oral azithromycin | 3 days | Inj Ceftriaxone,oral azithromycin | Double | 15 | 2 | Discharge | Typhoid Fever |
| 60 | 1138164 | - | - | - | Inj Ceftriaxone | 10 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 14 | 2 | Discharge | Paratyphoid Fever |
| 61 | 721137 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 8 | 1 | Discharge | Typhoid Fever |
| 62 | 1135839 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 12 | 2 | Discharge | Typhoid Fever |
| 63 | 1134515 | - | - | - | Inj Ceftriaxone | 5 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 12 | 2 | Discharge | Typhoid Fever |

| Sr. No | MRD | Age (months ) | Sex | DOA | DOD | Hospital stay ( days ) | Actual Weight (Kg) | Actual Height/ Length(cm) | Actual Head Circumference (cm) | Actual BMI | Expected Weight (Kg) | Expected Height/ Length(cm) | Expected Head Circumference (cm) | Expected BMI | Fever Duration ( days ) | Onset | Grade | Type | Rigors/Chill | Pain Abdomen | Characteristics of Pain Abdomen |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 64 | 979522 | 9 | female | 09-07-2021 | 17-07-2021 | 9 | 7.5 | 72 | 43.5 | - | 7.9 | 70 | 44 | - | 4 | acute | moderate | intermittent | not present | not present | - |
| 65 | 1134493 | 132 | male | 09-07-2021 | 16-07-2021 | 8 | 25 | 142 | - | 12.63 | 37 | 147 | - | 17.1 | 3 | acute | moderate | intermittent | not present | not present | - |
| 66 | 474983 | 51 | female | 05-07-2021 | 09-07-2021 | 5 | 14 | 98 | 50 | - | 16.5 | 105 | 49.5 | - | 3 | acute | moderate | intermittent | present | not present | - |
| 67 | 1127500 | 59 | feamle | 25-06-2021 | 02-07-2021 | 8 | 16 | 108 | 49 | - | 17 | 106 | 50 | - | 3 | acute | high | intermittent | present | present | mild , in epigastrium , no aggravating, relieving factors |
| 68 | 1156379 | 36 | female | 18-08-2021 | 24-08-2021 | 7 | 13 | 94 | 49 | - | 14 | 95 | 49 | - | 5 | acute | high | intermittent | not present | present | acute in onset , non radiating , no aggravating releiving factors |
| 69 | 1006016 | 23 | male | 21-08-2021 | 31-08-2021 | 11 | 11 | 85 | 46.5 | - | 11.5 | 86 | 47 | - | 4 | acute | high | intermittent | present | not present | - |
| 70 | 251136 | 60 | femlae | 28-08-2021 | 03-09-2021 | 7 | 15 | 103 | - | 14.15 | 16.2 | 108.5 | - | 14.2 | 5 | acute | high | intermittent | present | not present | - |

| Sr. No | MRD | Loose Stools / Vomitings | Loose stools /Vomitings EPISODES | Unconsciousness /Seizures | Past Drug History | Type of Antibiotic taken | Duration of Antibiotic | Vaccination History | Anaemia | Icterus | Edema: Face /Feet | HR | SBP | DBP | Temp | CFT | Chest | CVS | Liver /Spleen /Ascites | AVPU / GCS | Hb | MCV |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 64 | 979522 | present | Vomitings x 3 days , non bilious , non projectile , non blood stained ; Loose stools x 3 days , watery , non blood stained | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 124 | 118 | 60 | 100.4 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver spleen non palpable | 15 | 11.7 | 36.6 |
| 65 | 1134493 | present | Loose stools x 7 days , watery , non blood stained , | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 110 | 124 | 62 | 100.2 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | - | 15 | 11.6 | 36.6 |
| 66 | 474983 | present | Vomitings x 4 Hrs PTA , non bilious , non projectile , non blood stained | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 120 | 110 | 68 | 102.4 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 3 cm below RCM , spleen non palpable | 15 | 10 | 31.2 |
| 67 | 1127500 | present | Vomitings x 1 day , non bilious , non projectile , non blood stained | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 106 | 120 | 80 | 104 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 2 cm below RCM , spleen non palpable | 15 | 10.9 | 33.7 |
| 68 | 1156379 | not present | - | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 110 | 110 | 60 | 102 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 2 cm below RCM , spleen non palpable | 15 | 11.6 | 34.1 |
| 69 | 1006016 | present | vomitings x 3 days , non bilious , non projectile , 4 - 5 episodes /day , non blood stained | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 130 | 100 | 60 | 101 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 2 cm below RCM , spleen tip palpable | 15 | 5.1 | 18.9 |
| 70 | 251136 | present | vomitings x 1 day , 3 episodes per day , non bilious , non projectile | not present | no h/o previous antibiotic intake | - | - | Not vaccinated for typhoid | pallor + | not present | not present | 140 | 98 | 60 | 100.3 | 3 | b/l air entry + , No added sounds | S1 , S2 normal , no murmur | Liver 2 cm below RCM , spleen tip palpable | 15 | 12.4 | 36.1 |

| Sr. No | MRD | Anemia | TLC | N | L | M | E | Platelets | CRPq | ESR | LDH | SGOT | SGPT | ALP | TO | TH | AH | BH | Blood Culture | Azithromycin | cotrimoxazole | Ceftriaxone | Ciprofloxacin | Ofloxacin | Ampicillin | Cefixime | Cefuroxime | Chloramphenicol | Cefotaxime |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 64 | 979522 | Mild | 11.4 | 34.2 | 54.5 | 10.6 | 0.4 | 282000 | 40.9 | - | 367 | 61 | 28 | - | - | - | - | - | salmonella typhi | S | S | S | R | R | S | S | R | S | - |
| 65 | 1134493 | Mild | 11400 | 70.7 | 21.3 | 7.8 | 0 | 150000 | 38.5 | - | 325 | 35 | 21 | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 66 | 474983 | Mild | 9000 | 71.4 | 19.6 | 8.7 | 0 | 164000 | 91.5 | - | 356 | 52 | 26 | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 67 | 1127500 | Mild | 72000 | 58 | 37.1 | 4.3 | 0 | 100000 | 23.1 | - | 941 | - | 60 | - | 160 | 2560 ET | <20 | - | no growth | - | - | - | - | - | - | - | - | - | - |
| 68 | 1156379 | Mild | 86000 | 23.3 | 72.4 | 4 | 0 | 101000 | 15.1 | - | 576 | 127 | 93 | - | - | - | - | - | salmonella typhi | S | S | S | R | S | S | S | R | S | - |
| 69 | 1006016 | severe | 97000 | 55.4 | 40.9 | 3.4 | 0 | 108000 | 129 | - | - | 106 | 61 | 134 | - | - | - | - | salmonella typhi | S | S | S | R | R | S | S | R | S | - |
| 70 | 251136 | Mild | 6000 | 79.1 | 14.7 | 6 | 0.2 | 201000 | 22 | - | 417 | 22 | 68 | - | 640 | 320 | <20 | nil | salmonella typhi | S | S | S | R | R | S | S | R | S | - |

| Sr. No | MRD | Duration | Cefepime tazobactum | Duration | Ceftriaxone | Duration | Ofloxacin | Duration | Ciprofloxacin | Duration | Aminoglycosides | Duration Of antibiotics Intake | Antibiotics | No of Antibiotics | Days of Deffervesence of Fever | Deffervesence of Fever group | Outcome | FINAL DIAGNOSIS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 64 | 979522 | - | - | - | Inj Ceftriaxone | 7days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 10 | 2 | Discharge | Typhoid Fever |
| 65 | 1134493 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 9 | 1 | Discharge | Typhoid Fever |
| 66 | 474983 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | oral azithromycin | 5 days | Inj Ceftriaxone,oral azithromycin | Double | 9 | 1 | Discharge | Typhoid Fever |
| 67 | 1127500 | - | - | - | Inj Ceftriaxone | 8 days | - | - | - | - | oral azithromycin | 8 days | Inj Ceftriaxone,oral azithromycin | Double | 10 | 2 | Discharge | Enteric Fever |
| 68 | 1156379 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 13 | 2 | Discharge | Typhoid Fever |
| 69 | 1006016 | - | - | - | Inj Ceftriaxone | 10 days | - | - | - | - | oral azithromycin | 5 days | Inj Ceftriaxone,oral azithromycin | Double | 10 | 2 | Discharge | Typhoid Fever |
| 70 | 251136 | - | - | - | Inj Ceftriaxone | 7 days | - | - | - | - | - | - | Inj Ceftriaxone | Single | 11 | 2 | Discharge | Typhoid Fever |

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The Principal,
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**Subject:** **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 22.01.2021 has approved the plan of thesis of **Dr. Disha Joshi**, a student of your college for **MD Paediatrics** along with the names of Supervisor/Co-Supervisor as under:-

**Topic Plan of Thesis**
Clinical profile and antibiotic use in children with enteric fever

Supervisor
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Dept. of Paediatrics,
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Co-Supervisor
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The student has to submit the three copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,( if any).

S P Singh

Dr. S P Singh MS(Oph)
Controller of Examinations

*Note :*

1. ***If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.***
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

# CLINICAL PROFILE AND ANTIBIOTIC USE IN CHILDREN WITH ENTERIC FEVER

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

PAEDIATRICS

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

September, 2019

Dr. Disha Joshi

DEPARTMENT OF PAEDIATRICS
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

# ABSTRACT OF PLAN OF THESIS

| | |
|---|---|
| TITLE | Clinical Profile and Antibiotic Use in children with Enteric Fever |
| DEGREE | MD Paediatrics |
| NAME OF THE CANDIDATE | Dr. Disha Joshi |
| SUPERVISOR | Dr. Deepak Bhat, Professor, Department of Paediatrics, DMC&H, Ludhiana |
| CO – SUPERVISOR | Dr. Veenu Gupta, Professor, Department of Microbiology, DMC&H, Ludhiana<br>Dr. Gurdeep Singh Dhooria, Associate Professor, Department of Paediatrics, DMC&H, Ludhiana |
| INSTITUTION | Dayanand Medical College & Hospital, Ludhiana |
| UNIVERSITY | Baba Farid University of Health Sciences, Faridkot |

**INTRODUCTION:** Typhoid fever is a community acquired systemic infection which continues to be a public health problem in developing countries including India. It is more common in resource limited overcrowded communities with poor access to sanitation. Multidrug resistant strains are prevalent worldwide and have previously caused outbreaks in India also.

**AIM OF STUDY:** 1) To study clinical profile of children with Enteric Fever.
2) To study Antibiotic use and outcome in children with Enteric Fever.

**MATERIALS & METHODS:** This descriptive study will be conducted in the departments of Paediatrics and Microbiology, Dayanand Medical College and Hospital, Ludhiana, Punjab, India. All patients who meet the case definition as described below would be included in the study. Those who do not give consent will be excluded. This study will be done over a period of 18 months from January 2020 to June 2021. Probable case: A patient with fever (38°C and above) that has lasted for at least three days, with a clinically consistent case with positive serodiagnosis but without S. Typhi isolation. The study will be approved by the Institutional Ethics Committee of DMCH. Blood cultures: Blood cultures will be done for all the patients included in the study using Bact Alert automated system as per manufacturer's instructions. Serological tests: Widal Test

**CLINICAL SIGNIFICANCE:** The problem is compounded by the increasing antimicrobial resistance to the first line antibiotics used for the enteric fever. Multidrug resistant strains are prevalent worldwide and have previously caused outbreaks in India also. In recent years, there has been an increase in fluoroquinolones resistance because of which ciprofloxacin is no longer the empirical choice of treatment in our country. Hence the need to undertake this study.

**KEYWORDS:** Enteric fever, children, blood culture, widal test.

Disha Joshi (Signature) Candidate | (Signature) Co-supervisor | (Signature) Co-supervisor | (Signature) Supervisor | (Signature) Principal

## CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"CLINICAL PROFILE AND ANTIBIOTIC USE IN CHILDREN WITH ENTERIC FEVER"** exist in the Department of Paediatrics, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

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# APPROVAL PROFORMA
# BY
# RESEARCH & ETHICAL COMMITTEE
# DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

| | |
|---|---|
| **Name of candidate** | Dr. Disha Joshi |
| **Department** | Paediatric |
| **Topic of Thesis** | Clinical Profile and Antibiotic Use in children with Enteric Fever |
| **Likely date of appearing in PG examination** | May 2022 |
| **Date of enrollment** | 7th May, 2019 |
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| | Dr. Gagandeep Singh<br>(Secretary, Ethics Committee<br>Professor & Head, Neurology) |

**Approved: Yes / ~~No~~**

**Dr. Sandeep Puri**
**Chairperson**
**Research Committee**

Chairperson
Research Committee

**Approved: Yes / ~~No~~**

**Prof. Arvind Malhotra**
**Chairperson**
**Ethics Committee**

Chairperson
Ethics Committee

# BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

## PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

| | | |
|---|---|---|
| 1 | NAME OF THE CANDIDATE AND ADDRESS | Dr. Disha Joshi<br>Flat No.A 08, Apoorva Apartments, Plot No.14, Sector No.5, Dwarka, New Delhi. |
| 2 | NAME OF THE INSTITUTE | Dayanand Medical College and Hospital, Ludhiana |
| 3 | COURSE OF STUDY AND SUBJECT | MD Pediatrics |
| 4 | DATE OF ADMISSION OF COURSE | 7th May,2019 |
| 5 | TITLE OF THE TOPIC | Clinical Profile and Antibiotic Use in children with Enteric Fever |

## 6. BRIEF RESUME OF THE INTENDED WORK

### 6.1 NEED FOR THE STUDY

Typhoid fever is a community acquired systemic infection which continues to be a public health problem in developing countries including India. It is more common in resource limited overcrowded communities with poor access to sanitation. Although the infection can occur at any age, the higher incidence in children reflects the active transmission in a community. Late presentation to health care facilities, lack of appropriate diagnostic facilities, reliance on suboptimal tests and use of widespread antibiotics in the community are major issues concerning the appropriate management.

The problem is compounded by the increasing antimicrobial resistance to the first line antibiotics used for the enteric fever. Multidrug resistant strains are prevalent worldwide and have previously caused outbreaks in India also.

In recent years, there has been an increase in fluoroquinolone resistance because of which ciprofloxacin is no longer the empirical choice of treatment in our country. Hence the need to undertake this study.

Enteric fever can lead to increase in complications and morbidity if not treated with appropriate antimicrobial agents. The effective treatment of typhoid fever is becoming increasingly difficult in India due to the emergence of ciprofloxacin resistance compounded by the fact that ceftriaxone, which is presently the drug of choice for treatment, has started to show an increasing trend of minimum inhibitory concentration (MIC) values against Salmonella entericaserovarTyphi and S. entericaserovarParatyphi A.

In view of such a problem of emerging antimicrobial resistance, prevention of disease becomes a priority in public health. To guide public health interventions, it is important to monitor the trends of the disease, causative agents and their antimicrobial susceptibility. Some of the major issues responsible for incomplete information on the actual burden of typhoid fever in India are the uneven disease distribution of this infection in different geographical areas, occurrence of outbreaks from time to time and lack of blood culture facilities across health-care centres in India for actual estimates of disease burden.[1,2]

It is possible that the emerging antibiotic resistant strains, under the selective pressure of antibiotic use, could be the reason that only patients failing to respond to empirical treatment visit tertiary care hospitals. Therefore the culture positive cases of typhoid fever represent only a small proportion of total number of cases in a community and this can skew the antimicrobial susceptibility data towards resistance. Hence, there is a need for continuous surveillance to inform clinicians for better management of infections, availability of blood cultures in the peripheral hospitals to understand the actual burden of the disease and for government policymakers for vaccine strategies, especially in light of the increase in S. Paratyphi A prevalence. Safe supply water, personal hygiene and effective antibiotic policies can help us to control the disease and hence reduce antimicrobial resistance.[3,4]

In the present global scenario of changing antimicrobial resistance pattern, continuous surveillance for resistance and characterisation is important because it will inform the geographical areas which need immediate alterations with regard to the travel and deciding vaccine strategies.

## 6.2 REVIEW OF LITERATURE

Most common etiological agent of enteric fever is S. Typhi causing the majority of cases from July to October in our region. MIC to ceftriaxone in typhoidal salmonellae is creeping towards resistance and more data are needed to understand the azithromycin susceptibility.

The emerging antibiotic resistant strains, under the selective pressure of antibiotic use, could be the reason that only patients failing to respond to empirical treatment visit tertiary care hospitals. Therefore the culture positive cases of typhoid fever represent only a small proportion of total number of cases in a community and this can skew the antimicrobial susceptibility data towards resistance. Hence, there is a need for continuous surveillance to inform clinicians for better management of infections, availability of blood cultures in the peripheral hospitals to understand the actual burden of the disease and for government policymakers for vaccine strategies, especially in light of the increase in S. Paratyphi A prevalence. Safe supply water, personal hygiene and effective antibiotic policies can help us to control the disease and hence reduce antimicrobial resistance.[5]

Most common etiological agent of enteric fever is S. Typhi causing the majority of cases from July to October in our region. MIC to ceftriaxone in typhoidal salmonellae is creeping towards resistance and more data are needed to understand the azithromycin susceptibility.[6]

Typhoid fever is most commonly observed with unhygienic practices and eating of unhealthy outside food. This major public health issue can be tackled by bringing awareness among people regarding disease transmission and its various preventive measures.[7]

The high rate of MDR, as well as almost universal resistance to nalidixic acid and reduced sensitivity to ciprofloxacin of the bacterial strains during this study period, limits treatment choices to third-generation cephalosporins (ceftriaxone and cefixime) and azithromycin.[8]

Atypical presentations are seen in typhoid fever patients so we need to be cautious about it, clinical symptoms and signs can vary with different regional studies, may be attributed to use of empirical oral antibiotic that alter the clinical presentation of enteric fever. Low culture positivity is due to prior or ongoing antibiotic treatment outside hospital setting. Leucopenia could be an

important marker of typhoid. Ceftriaxone is important available cephalosporin for sensitive cases. Combination treatment was used to treat persistently febrile child.[9]

The antibiotic sensitivity pattern in the patients showed a high level of resistance to fluoroquinolones at 29.2%. Decreasing susceptibility of Salmonella typhi to ciprofloxacin has been well documented in several studies,[10-12] and is indicative of the effects of indiscriminate use of this group of antibiotics. Sensitivity to cephalosporins in the current study was high, as reported in other studies. The change in the resistance patterns of chloramphenicol, ampicillin and cotrimoxazole is noteworthy. The following resistance pattern of serotype Typhi strains was observed from Kolkata: chloramphenicol, 13%; ampicillin, 13%; amoxicillin-clavulanic acid, 0%; cotrimoxazole, 15%; ciprofloxacin, 10%; ofloxacin, 2%; and ceftriaxone, 0%. A significant decrease over the years in resistance to chloramphenicol, ampicillin and cotrimoxazole was noticed ($P<0.0001$). Sensitivity to the conventional antibiotics, especially chloramphenicol is high (92.5%). Similar findings were reported in other studies. Our study thus confirms a roll-back sensitivity of Salmonella typhi to chloramphenicol.

Mean duration of fever was 6.9±2.1 days and the mean duration of hospital stay was 5.5±1.4 days.

Most of the cases were >5 years age (80%) with only 20% children being <5 years of age. There was no sex difference with girls and boys ratio being 1.14:1. Fever was the most consistent symptom (100%) followed by malaise (78.33%), anorexia (75%), vomiting (60%), chills (58%), diarrhea (53.33%) etc; constipation and joint pain were rare. Among the signs, coated tongue was seen in 70%, splenomegaly in 63.33%, hepatomegaly in 53.33% and hepatosplenomegaly in 36.66% cases. Rose spots, icterus as well as complications were not seen.

CBC changes were non-specific. Widal test was positive in only 71.7% of culture positive cases. Incidence of MDTRF was high (21.7%). 3rd generation cephalosporins were sensitive in 80-90% cases. Some strains were resistant to most of the drugs including 3rd generation cephalosporins, which is worrisome. Re-emergence of sensitivity to 1st line drugs chloramphenicol and TMP-SMZ is a good news.[13]

Among the 106 individuals who were culture positive for Salmonella typhi, majority [83 (78.3%)] were males and 23 (21.7%) were females. Majority of the patients were (55.7%) in the age group of 15-30 years, and were students (39.6%). The mean age of the patients was 28.8 years (SD 1.32). People engaged in skilled and semiskilled occupation constituted 46%, while housewives [9 (8.5%)] and children [4 (3.8%)] formed the rest of the study population in addition to students. The average duration of hospital stay was 8.7 days. Fever was present in all the patients. Headache, vomiting, abdominal pain and diarrhea were the common associated symptoms seen in 63 (59.4%), 30 (28.3%), 21 (19.8%) and 29 (27.4%) patients, respectively. Splenomegaly was seen in 47 (44.3%), hepatomegaly was present in 42 (39.6%) while hepatosplenomegaly was seen in 23 (21.7%). Abdominal tenderness was another common presenting sign [23 (21.7%)]. Widal was concomitantly positive in 73 (68.9%) cases. Liver enzymes (alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase) were raised in 52 (49.1%) patients. Complications were very few. Only one patient each had gastrointestinal bleed, gastrointestinal perforation, myocarditis and encephalitis as complications. The outcome was favorable, with 92.5% patients recovering from the illness. Relapse of the disease was seen among two (1.9%) cases, while five patients (4.7%) were discharged against medical advice. Antibiotic sensitivity for cephalosporins was 96.2% while antibiotic resistance was 29.2% with fluoroquinolones. Sensitivity to chloramphenicol was 92.5%, ampicillin 85% and sulphonamides 82.1%. Majority [50 (47.6%)] of the typhoid cases were treated with ceftriaxone. Another five (4.8%) cases were treated with quinolones. A combination of ceftriaxone and quinolones were given for 32 cases (30.5%). Rest of the patients were treated with a combination of antibiotics, including beta lactams, quinolones, aminoglycosides and sulphonamides. The overall outcome of the patients was good; 99 (92.5%) patients recovered without any complications. The antibiotic sensitivity pattern in the patients showed a high level of resistance to fluoroquinolones at 29.2%. Decreasing susceptibility of Salmonella typhi to ciprofloxacin has been well documented in several studies,[10,14-16] and is indicative of the effects of indiscriminate use of this

group of antibiotics. Sensitivity to cephalosporins in the current study was high, as reported in other studies.

## 7. MATERIALS AND METHODS

### 7.1 Source of Data

All inpatients who are either confirmed cases or probable cases, irrespective of the age of children, admitted under the paediatric departments in DMCH.

### 7.2 METHOD OF COLLECTION OF DATA

This descriptive study will be conducted in the departments of Paediatrics and Microbiology, Dayanand Medical College and Hospital, Ludhiana, Punjab, India.

**Inclusion Criteria:** All the children who come to paediatrics services with a diagnosis of enteric fever as per the case definition will be included in the study after informed written consent .

**Exclusion Criteria** :. Those who do not give consent will be excluded.

**Duration Of Study** :This study will be done over a period of 18 months from January 2020 to June 2021.. Based on the pre-defined proforma, patient's demographic and clinical details would be recorded.

**Case definitions**: This will be based on Paediatric department, DMCH, Ludhiana, protocols adapted from the WHO and Indian Academy of Pediatrics (IAP) guidelines.

**Confirmed case**: A patient with fever (38°C and above) that has lasted for at least three days, with a laboratory-confirmed positive culture (blood, bone marrow and bowel fluid) of Salmonella Typhi or S. Paratyphi A.

Probable case: A patient with fever (38°C and above) that has lasted for at least three days, with a clinically consistent case with positive serodiagnosis but without S. Typhi and S .Paratyphi isolation.

**Sample Collection**

Under all aseptic precautions, amount of blood will be withdrawn from antecubital vein with disposable syringe and will be inoculated directly into commercially prepared BACTEC 9240 or Bact /Alert culture bottles. 1 – 3 ml of blood will be collected in a vacutainer without EDTA .Serum will be separated by centrifugation at room temperature.

**Sample Processing**: Samples received in Microbiology lab will be processed as per standard protocols.

Blood specimen will be processed in the Bactec or Bact -T / Alert microbial detection system. The blood culture bottles will be loaded in the instrument and incubated for a maximum period of 7 days or till the bottle indicates positive by the system and time to show positive will be noted.

Bottles will be placed into receiving wells that will be monitored once every 10minutes.

Processing of blood culture positive bottles:

Smears will be prepared from the positive blood culture bottles and gram staining of the smears will be done.

Also the positive bottles will be subcultured on blood agar and MacConkey agar plate. The plate will be incubated at 37 degrees centigrade for 18 – 24 hours.

Antibiotic sensitivity testing will be done of Salmonella isolates for antibiotics and MIC will be calculated.

Sensitivity against these antibiotics will be observed.

Azithromycin

Ceftriaxone

Ciprofloxacin

Ofloxacin

Ampicillin

Cefixime

Cefuroxime

Chloramphenicol

Serodiagnosis by Widal Test:

It is a tube agglutination test for the measurement of H and O agglutinins for Typhoid and Paratyphoid bacilli in the patient's sera.

**Procedure**: Equal volume of serial dilutions of the serum and the H and O Ag are mixed in Dreyer 's and Felix agglutination tube respectively and incubated in water bath at 37 degrees centigrade overnight .

Control tubes containing Ag and Normal saline are checked for agglutination The agglutination titres of the serum are read.

H agglutination leads to formation of loose, cotton woolly clumps

O agglutination is seen as disc like pattern ( granular matt ) at the bottom of the tube.

If there is no evidence of agglutination in Felix and Dreyer 's tube ,then titre for TO , TH ,AH , BH is reported as < 20.

**OUTCOME**

To treat a patient with enteric fever by using antibiotics and to study the antimicrobial resistance profile of Salmonella.

**STATISTICAL ANALYSIS**

Data were described in terms of range; mean ±standard deviation (± SD), frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

**7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.**

This study requires investigations in all inpatients. Hemogram, Liver function tests, Widal test, Blood culture and senstivity pattern.

**7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?**

Attached herewith

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16. Bhutta ZA. Current concepts in the diagnosis and treatment of typhoid fever. BMJ. 2006;333:78-82.

# PROFORMA

Name: MRD No.

| Age | Sex |
|---|---|
| DOA | DOD |

Residence:

Month:

Hospital stay:

| Anthropometry. | Actual | Expected. | Remarks |
|---|---|---|---|
| Weight (Kg) | | | |
| Height/Length(cm) | | | |
| Head Circumference (cm) | | | |
| BMI | | | |

**Fever**

1. Duration
2. Onset
3. Grade
4. Type
5. Rigors /Chills

**Signature of candidate :** **Signature of consultant:**

6. Pain Abdomen
7. Loose stools /Vomitings
8. Unconsciousness /Seizures

**Past Drug History**

**Type of Antibiotic taken**

**Duration of Antibiotic**

**Vaccination History**

**GPE**

- Anaemia /Icterus/Edema: Face /Feet
- Vitals : HR : BP : Temp .
- CFT
- Chest:
- CVS :
- P/A : Liver /Spleen /Ascites
- CNS :AVPU / GCS

**INVESTIGATIONS**

| | |
|---|---|
| **Hb/MCV :**<br>**Anaemia** | **Septic markers**<br>**CRPq**<br>**ESR** |
| **TLC**<br>**N/L/M/E** | **LFTs**<br>**TSB/DSB:** |



**Signature of candidate :** **Signature of consultant:**

| | |
|---|---|
| | **ALP** |
| **Platelets** | **Widal Titers**<br><br>**TO /TH/AH/BH** |

**Blood culture and sensitivity**

| |
|---|
| |

**Treatment**

**Antibiotics Used**

| **Type of Antibiotic** | **Duration of antibiotic used** |
|---|---|
| Cefotaxime | |
| Ceftriaxone | |
| Ofloxacin | |
| Ciprofloxacin | |
| Aminoglycosides | |

**Days of Defervescence:**

**Outcome**

**DOR/LAMA**

- FINAL DIAGNOSIS



**Signature of candidate :** **Signature of consultant:**

## INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....
am willing to participate in the study **"CLINICAL PROFILE AND ANTIBIOTIC USE IN CHILDREN WITH ENTERIC FEVER"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

..... .....
Signature of the Witness Signature of the patient

Name:

**Signature of Candidate** **Signature of Supervisor**

# मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य **"CLINICAL PROFILE AND ANTIBIOTIC USE IN CHILDREN WITH ENTERIC FEVER"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____
गवाह के हस्ताक्षर
नाम:

_____
रोगी के हस्ताक्षर/अंगूठे का निशान
नाम:

_____
अन्वेषक के हस्ताक्षर

_____
विद्यार्थी के हस्ताक्षर

# ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"CLINICAL PROFILE AND ANTIBIOTIC USE IN CHILDREN WITH ENTERIC FEVER" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____
ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ

_____
ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____

ਮਿਤੀ_____

ਪਤਾ _____

ਪਤਾ _____

_____
ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____
ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ

## PATIENT'S PARENT/GUARDIAN CONSENT FORM

Date: ____/____/____

I .....F/o, M/o ..... R/o ..... am willing to let my child participate in the study entitled Bed **"CLINICAL PROFILE AND ANTIBIOTIC USE IN CHILDREN WITH ENTERIC FEVER"**. The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason. This will not affect my treatment and investigation of my child.

Signature of the Witness
Name:

Signature/Thumb Impression of guardian
Name:

Signature of the Supervisor

Signature of Candidate

## ਮਰੀਜ ਦੇ ਮਾਤਾ/ਪਿਤਾ ਦਾ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ __/___/____

ਮੈਂ _____ ਪਿਤਾਮਾਤਾ _____,

ਵਾਸੀ _____

ਆਪਣੇ ਬੱਚੇ ਦੇ ਇਸ ਅਧਿਐਨ ਵਿੱਚ ਹਿੱਸਾ ਲੈਣ ਤੇ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿੱਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈਂ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈਂ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ/ਚਾਹੁੰਦੀ ਹਾਂ ਕਿ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂੰ ਕਿਸੇ ਵੀ ਤਰ੍ਹਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀਂ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂੰ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂੰ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂੰ ਇਸ ਖੋਜ ਵਿੱਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆਂ ਹੈ ਅਤੇ ਮੈਨੂੰ ਇਹ ਯਕੀਨ ਹੈ ਕਿ ਇਹ ਖਤਰਾ ਬਹੁਤਾ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂੰ ਇਸ ਖੋਜ ਕੰਮ ਵਿੱਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ-ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈਂ ਇਸ ਖੋਜ ਕੰਮ ਵਿੱਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇਂ ਵਾਪਸ ਲੈ ਸਕਦਾ/ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਬੱਚੇ ਦੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀਂ ਹੋਵੇਗਾ।

| | |
|---|---|
| _____ | _____ |
| ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ | ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ |
| ਮਿਤੀ _____ | ਮਿਤੀ _____ |
| ਪਤਾ _____ | ਪਤਾ _____ |
| _____ | _____ |
| ਨਰੀਖਕ ਦੇ ਹਸਤਾਖਰ | ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ |

# मरीज के माता/पिता का अनुमति फार्म

तिथि ___/___/___

मैं _____ पिता/माता/_____ वासी _____, अपने बच्चे के इस शोधकार्य में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ कि स्वीकृत देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है कि यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामूली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे बच्चे के इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ गवाह के हस्ताक्षर

_____ मरीज के माता/पिता के हस्ताक्षर

तिथि _____

पता _____

_____

_____

_____ नरीक्षक के हस्ताक्षर

_____ प्रत्याक्षी के हस्ताक्षर